Archives of Dermatology and Syphilology

VOLUME 37 MAY 1938 NUMBER 5

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EARLY EPIDERMAL NEOPLASIA: DESCRIPTION AND INTERPRETATION

THE THEORY OF MUTATION IN THE ORIGIN OF CANCER

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The clinician's dealings with cancer are, in general—and regrettably so—associated with what one may call advanced disease. The concepts of the earliest and smallest lesions are vague even among experts. I have been interested, perhaps impractically, in lesions that are clinically, at the time examined, of no apparent consequence. I shall present material concerned especially with these small and early lesions.

Cancer is a cellular disease. It begins in one or at the most in only a few cells.

That cancer is a cellular disease is made evident by a number of facts. All animals and perhaps plants are subject to cancer. Cancer has been observed in human beings, rats, mice, chickens, dogs, cats, horses, fruit flies and many other creatures. On apples mole-like lesions composed of irregular masses of cells, which differ from normal somatic cells in the inability of the scab fungus to grow on them, have been described by Kostoff and Kendall.[1] Gall formations and fasciations occurring sporadically in plants and analogous to atypical growths in animals have been remarked by Jones.[2] A. J. Mix, professor of botany at the University of Kansas, states that crown gall in apples is certainly of bacterial origin. Stark [3] observed a tumor occurring in Drosophila, grew its cells in tissue culture and reinoculated them into the flies with positive results. The fact of metastasis speaks for itself. When a particle of tumor tissue removes itself from the parent tumor and settles and proliferates in a new locality, the progeny are identical

Read before the Section on Dermatology and Syphilology at the Eighty-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 11, 1937 (appropriate modifications added April 28, 1938).

1. Kostoff, D., and Kendall, J.: J. Genetics **21**:113, 1929.
2. Jones, D. F.: Science **81**:75 (Jan. 18) 1935.
3. Stark, M. B.: J. Exper. Zoöl. **27**:509, 1918-1919.

with those cells of the parent from which they were derived. Schmidt [4] injected an emulsion of tumor tissue intravenously and found that a small proportion of the cancer emboli are able to become fixed and reproduce themselves in new places. Tyzzer's [5] experiments proved for transplanted carcinoma in mice that if a tumor is massaged daily metastases to the lungs are much more frequent than if that operation is omitted. Marsh [6] confirmed the finding in spontaneous cancer of the breast in these animals. Kost [7] reported that cancer emboli in human lungs may enter without reaction, with thrombus formation and destruction of neoplastic cells or with formation of a metastatic colony; of twelve patients with cancer, two had pulmonary metastases; five had demonstrable tumor cells in the lungs, and five were free from such pulmonic invasion.

As Lockhart-Mummery [8] pointed out, tumor cells are species specific, and they cannot be grafted to a different animal; there exist varieties not only for each species but for each type of tissue. Their essential difference from normal is one of behavior, not of apparent structure, for their resemblance to normal as individual cells is usually close.

Countless experiments in transplantation have succeeded. I mention particularly those of Mottram,[9] working with neoplasia produced in mice by the application of tar to the skin. Ludford [10] stated in 1930 that twenty-four different transplantable mammalian tumors were under observation in the laboratory of the Imperial Cancer Research Fund in London, and that two mouse tumors had been maintained unaltered for twenty-three years. Pinkus [11] isolated and kept pure strains of human myxofibrosarcoma, ependymoma and glioblastoma in vitro for as long as nine months but was unable to grow squamous cell carcinoma. Crosti [12] reported failure in attempted autotransplants of ten basal cell, three squamous cell and three other malignant growths of the skin in the human being.

While such facts may be mustered as evidence of the cellular nature of cancer, the opinions of other authors are corroborative. Broders [13]

4. Schmidt, M. B.: Die Verbreitungswege der Karzinome und die Beziehung generalisierter Sarkome zu den leukämischen Neubildungen, Jena, Gustav Fischer, 1903.

5. Tyzzer, E. E.: J. M. Research **28**:309, 1913.

6. Marsh, M. C.: J. Cancer Research **11**:101, 1927.

7. Kost, G. F. W.: Ztschr. f. Krebsforsch. **43**:291, 1936.

8. Lockhart-Mummery, J. P.: Brit. M. J. **1**:785 (April 30) 1932; **1**:867 (April 27) 1935.

9. Mottram, J. C.: Am. J. Cancer **22**:801, 1934.

10. Ludford, R. J.: Scient. Rep. Invest. Imp. Cancer Research Fund **9**:99, 1930.

11. Pinkus, H.: Am. J. Cancer **26**:521, 1936; **29**:25, 1937.

12. Crosti, A.: Gior. ital. di dermat. e sif. **77**:145, 1936.

13. Broders, A. C.: J. A. M. A. **99**:1670 (Nov. 12) 1932.

stated "Carcinoma, regardless of etiology, is a primary disease of the epithelial cells, and all other phases and sequelae, though of great importance, are in reality of secondary nature." In Savatard's [14] study of small epidermal anomalies he showed that cancer may be diagnosed while still in an early stage. I [15] have described the beginnings of small cancerous lesions on previously unaltered human skin, where the earliest visible manifestations are circumscribed dyskeratotic lesions which progress by continuous evolution into large and destructive tumors. A summary of Gye's report [16] averred:

> It is now known that cancer begins as a change in a single normal cell or small group of normal cells, which acquire the power of autonomous growth . . . the factors which confer on a cell the property of autonomous growth reside within it and cannot be attributed to agents acting from without, though these may be a remote cause. . . . They prepare the area . . . they produce a "precancerous" condition.

Transplantation of tumor cells by the scalpel has been recognized by surgeons for many years. Saphir [17] was able actually to demonstrate such cells on a knife used to cut through carcinoma of the breast.

A solitary living cell may possess all the attributes of cancer within itself.

Since it is a cellular disease, one can investigate squamous carcinoma of the skin as an embryologist would, by studying small lesions of brief duration and comparing them with more advanced ones. I present histologic evidence of the manner of commencement of squamous carcinoma in the human skin, showing that the tumor cells even in small numbers differ distinctly from normal ones in both appearance and behavior, that small lesions differ from large ones only quantitatively and that tumor growth actually, as well as hypothetically, seems to progress from initial alteration of one or a few cells. The material is spontaneous and human; the lesions are from medical practice.

METHOD OF INVESTIGATION

The photomicrographs have been made by exposing successive areas of the slides, the movement being accomplished with a mechanical stage. The negatives, made on cut film, were then arranged in order, pieced together and printed on sensitive paper with an enlarger.

Entire lesions were excised with wide margins and sectioned and studied as a whole, rather than in bits by the less instructive method employed in biopsy. The specimens are in every way comparable to the histologic sections of whole breast and of whole organ so expertly made by the late Thomas Hamilton of the Royal College of Physicians Laboratory, of Edinburgh, Scotland.

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14. Savatard, L.: Brit. J. Dermat. **32**:375, 1920.
15. Sutton, R. L., Jr.: J. A. M. A. **104**:433 (Feb. 9) 1935.
16. Gye, W. E.: Brit. M. J. **2**:1276 (Dec. 19) 1936; J. A. M. A. **108**:652 (Feb. 20) 1937.
17. Saphir, O.: Surg., Gynec. & Obst. **63**:775, 1936.

In the following discussion statements regarding clinical, or grossly visible, and histologic, or microscopic, aspects of lesions will be intermingled. I believe that to those to whom a microscope is not a curiosity this method will be clarifying rather than confusing. Cellular pathology is simply pathology with ocular refinement. The essential background for comprehension of the argument is familiarity with these facts: All living creatures are composed of cells; at one time in its life each living creature existed in its entirety in one solitary cell, a fertilized ovum; all subsequent developments depend on mitosis of this cell and mitosis of its progeny; as Reimann and Hall [18] pointed out, cells have three interlocking but fairly independent capabilities, proliferation, differentiation and organization; all tissues are collections of cells in various arrangements; the unit of any mass of tissue is the cell; the properties of any grossly visible cellular collection are the properties en masse of individual cells spatially associated with each other and therefore to some extent interdependent.

The most minute scaling anomaly on the keratosic face of a blue-eyed, sun-sensitive Kansas farmer comes into existence on previously normal skin. It is roughly circular, impalpable and slightly browner than the surrounding pink skin. It is an epidermal lesion, and the histologic abnormality is seen in the epidermis or at the dermo-epidermal junction.

Mottram [9] painted mice daily with tar and observed the earliest visible lesions about one hundred or one hundred and fifty days after beginning the experiment. These lesions, epidermal anomalies, when first visible were from 1 to 3 mm. in diameter, and they began from that point visibly to enlarge and to become warty or infiltrative.

In human lesions in this stage the microscope shows a new growth of epidermal cells in the epithelium or at the dermo-epidermal junction. The photomicrographs (fig. 1, *A* and *B*) show what is going on. Cells differing from normal ones are replacing, infiltrating, undergrowing and overgrowing the normal epidermal cells. The new kind are homogeneous, grow as a sheet (one must keep in mind the three dimensions), replace the normal epidermal cell layer completely in the center of the lesion and undergrow the normal cells from the center to the border. The new cells grow faster than the normal ones. The proof of this lies in the fact that while normal epidermal cells continually proliferate, cornify and scale off uniformly over the whole surface of the body, these new cells constitute a lesion which is scaling faster than normal; if they were not outgrowing the normal cells a visible scale would not develop.

18. Reimann, S. P., and Hall, E. M.: Arch. Path. **22**:55 (July) 1936.

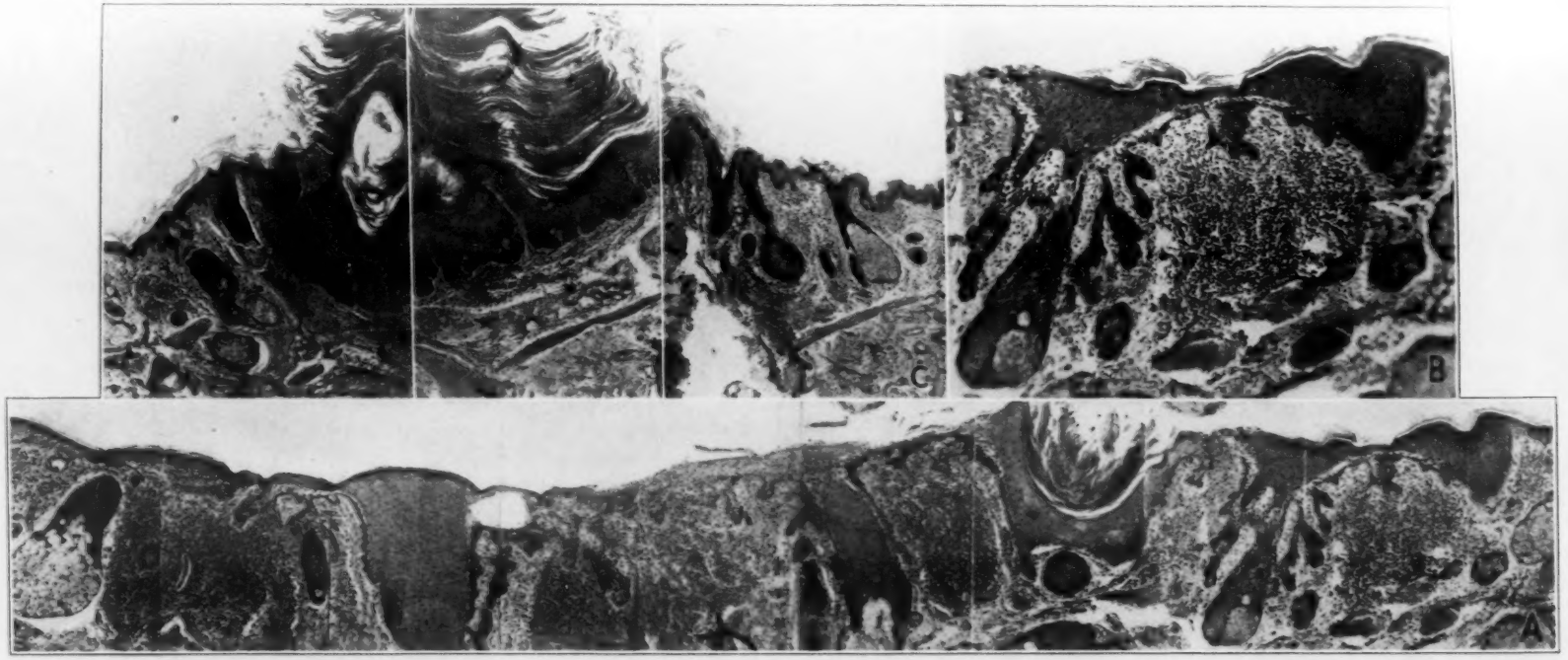

Fig. 1.—*A*, a scaly brown early squamous cell carcinoma 4 mm. in diameter from the helix of the ear of a man 61 years of age, with blue eyes and fair complexion. The neoplastic cells have completely replaced the epidermis in the central part of the lesion. They are undergrowing and surrounding normal epithelium as they spread centrifugally. On mucous membrane this would be erythroplakia. This specimen is an example of type II(a) (entire lesion, × 33). *B*, spread of cancerous cells at the dermo-epidermal junction in the form of an expanding sheet, which buckles into the dermis, produces by shearing the separation of normal from abnormal and terminates abruptly at the edge (× 60). *C*, a lesion with translucent yellowish horn surmounting a thickened epithelial base, from the face of a blond farmer aged 50 years. The multilayered abnormal epithelium is strongly coherent and growing slowly. This specimen is an example of type I(a) (× 25).

NORMAL RATE OF EPIDERMAL REPRODUCTION

To obtain a measure of the rate of reproduction of normal epidermal cells, I painted several areas of my skin with a solution of silver nitrate of a strength (10 per cent aqueous) that did not irritate but merely identified unmistakably the horny cells of those areas. I found that from seven to eleven days was necessary for their replacement in different areas, the period being somewhat dependent on friction, for the hands, frequently washed, peeled soonest. This is the time, then, that is required for the proliferating cells to replace some eight layers of hornifying cells. By allowing 1.5 square meters for the body surface, 25 square microns for each basal cell and a mitosis for each basal cell each day in order to account for the replacement of about eight layers in eight days, one can estimate that about 60,000,000,000 mitoses a day occur in the epidermis, over many years in each human being under normal conditions! While I make no claim to first digit accuracy for this number, 60,000,000,000, yet the number of cellular reproductive events is of that order. Thuringer [19] has investigated mitosis in normal human epidermis with results numerically more accurate.

DESCRIPTION OF EARLY EPIDERMAL NEOPLASIA

A lesion composed of altered cells must in order to exist be composed of cells reproducing at a greater rate than normal. If the scaly lesion scales off each week, its cells are presumably undergoing mitosis about twice as fast as the normal ones do. Suppose, tentatively, that the alteration began in one solitary cell. What is the predictable course of events? The progeny of this cell, growing faster than normal by two to one, would replace them, infiltrate and invade them, push them aside and grow among and under them, growing where epithelium is able to grow and using the host as a culture medium. The epidermal layer at the point of commencement would be the first replaced. The new cells might grow slowly or swiftly. They might be coherent and form a multilayered epidermal disk that expanded more rapidly than surrounding normal epidermis; they might push out centrifugally in a sheet, or they might grow expansviely without coherence.

Given the existence of neoplastic cells, it is my belief that their gross and microscopic appearance and behavior are properly analyzable in terms of two physical aspects: their rate of proliferation and their tendency to cling to one another. By coherence I mean a property which is much in evidence in the epithelium of a cutaneous horn, in contrast with its lack in the epithelium of those senile keratoses which bleed easily and scale off readily.

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19. Thuringer, J. M.: Anat. Rec. **28**:31, 1924; **40**:1, 1928.

I present photomicrographs of a number of individual epidermal blastomas which exemplify degrees of these two factors: speed of growth and cohesiveness of cells. The table shows a scheme of classifying the members of the series, most of which are depicted among the illustrations.

The following descriptions of types are generalizations of the specific examples:

Type I (a).—The new cells may be similar to the normal ones, outgrowing them only by a small differential rate, and strongly coherent. They resemble normal cells more than do faster growing neoplastic cells. They gradually replace the normal as a multilayered epidermal disk. This disk expands. It buckles not in a single layer but through its many layers and produces a warty growth, such as figure 1 *C* illustrates. The differences between normal and abnormal cells are not conspicuous, but there are real differences. These cells must be dif-

Classification of Blastomas

Type		(a) Slow Rate of Growth	(b) Fast Rate of Growth
I	Strong coherence	Cutaneous horn Quiescent senile keratoses Leukoplakia	Carcinoma with well developed pearls, slow to metastasize
II	Weak coherence	Progressive senile keratoses Intra-epidermal neoplasms Erythroplakia	Carcinoma with poorly developed pearls
III	No coherence	Intra-epidermal neoplasms Bowen's disease Slowly progressive Paget's disease	Highly malignant carcinoma Rapidly progressive Paget's disease

ferent, or they would not behave differently, would not produce an acanthotic layer of greater thickness than normal, would not cohere when cornified to make a scaly lesion and would not be irregularly arranged within the depths of the layer in cornifying whorls. In verruca vulgaris this does not occur; the cells in verruca are normal cells that are "sick," but here are abnormal cells that are living prosperously. Lesions composed of such cells comprise disks, in which expansion of the disk as a whole, due to a greater than normal rate of growth, results in warping, buckling and the formation of warty excrescences, or senile keratoses. On mucous membranes such growth when coherent heaps up cells, hides underlying blood and becomes leukoplakia.[19a] Since the differential rate of growth of the component cells is slow and since they cohere, the lesion is benign. The multilayered disk expands, warps and forms a papillated growth with a surface considerably larger than the surface it replaces. When the

19a. Leukoplakia is a symptom, not a diagnosis; sometimes leukoplakia is cancer (Schiller, W.: Am. J. Obst. & Gynec. **35**:17 [Jan.] 1938).

irregular, expanded involved surface is large enough, the constant proliferation suffices merely to furnish scale. Equilibrium is reached, and further clinical growth is no longer apparent. A balance is attained wherein the scaling of the large surface equalizes the rate of neoplastic growth, an excess rate which initially produced the visible lesion. Such growths are observed to be benign. They look benign under the microscope (fig. 1 *C*).

Type I (*b*).—While the cells are coherent, their rate of growth is greater. Such lesions as seen in figure 2 are the result. Instead of warping and buckling, the multilayered disk of replacing epithelium expands, invades and pushes outward as a rapidly growing warty structure or pushes into the dermis in coherent clumps undergoing central hornification; and the lesion is a cancer of Broders' least malignant group. The relative lack of malignancy is due to coherence, which prevents early metastasis, although the lesions may grow fast. These lesions are initially replacements of epidermis by speedily growing cells which tend to be coherent, resemble normal cells considerably but, growing more rapidly, invade in clumps, are called highly differentiated and are interpreted by pathologists as moderately malignant. The downgrowths, when developed, have well formed pearls, the epithelium being multilayered because of coherence. Narrow strands and invasions by isolated epidermal cells are not seen. Early lesions of this type are exemplified in figure 2.

Type II (*a*).—In these lesions the new cells spread as a sheet of the thickness at first of a single cell; the sheet warps and its cells proliferate with comparatively little coherence. These are senile keratoses that scale off readily or erythroplakias of mucous membranes, red because of the ease of scaling. They are called "precancerous" lesions; they are, in fact, cancerous already—early, superficial and requiring time to manifest those characteristics of cancer with which all clinicians are familiar, but cancerous, nevertheless. The sheet may expand comparatively slowly, in which case it can push its way centrifugally comparatively far before its buckling leads to deep invasion of the dermis.

The faster the rate of growth, the sooner downgrowth will occur. It is clinically true of early cutaneous carcinoma that the wider the surface extension before dermal invasion takes place, the more benign the lesion. (Witness Bowen's [20] disease and superficial basal cell epithelioma.) An evidence of difference from normal on the part of the cells in these neoplastic lesions is the fact that their metabolism evokes cellular infiltration and increased vascularity of the dermis.

20. Bowen, J. T.: J. Cutan. Dis. **30**:241, 1912.

Stryker,[21] among others, has pointed out the clinical significance of the zone of redness about senile keratosis. Such a zone implies activity, presages progression and prognosticates future clinical cancerousness—cancerousness which I aver is there at the time. In such lesions the spreading in a sheet gives rise to shearing stress along the junction of layers of normal and abnormal cells, due to the different rates of growth of normal and abnormal. In fixed preparations the layers tend to pull apart, an artefact manifest in figure 1, *A*.

In that photomicrograph the replacement of normal by abnormal is evident in the center of the lesion. This portion cannot be differentiated histologically from erythroplakia. This lesion was scaly because its component units were reproducing faster than normal. At the periphery of the scaling area the sheet of abnormal cells pushes its way along the dermo-epidermal junction, ensheathing the accessory structures of the skin, the fat glands and the hairs. The sheet has extended only to demonstrable end points. It is a colony of cells with a definite border. Growing speedily, the sheet expands, and it must buckle. The buckling produces downgrowths, which are the earliest anlages of horny pearls. When more cells have appeared and the downgrowths have become multilayered by cellular reproduction, the central portions cornify, for they are farthest from the nutrient supply, just as the external layers of normal epithelium cornify, being farthest from nutriment. Mekie,[22] studying normal and abnormal stratified squamous epithelium, showed that their respective necrobiotic alterations are analogous, the morphologic changes being products of nutrition rather than of differentiation. "Differentiation," which for Broders [23] is an important determinant of malignancy, is actually degeneration and death, manifested by flat cornification of epidermis or spherical cornification (pearls) within lumps of neoplastic epithelium. In rapidly growing tumors whose cells have little coherence, pearls are few and malignancy is great. As Mekie [22] said, the varied histologic appearance of tumor cells is not the expression of an inherent characteristic so much as it is the result of the interaction of a number of factors. These factors, I believe, include the immediate local environment of the cell, its stage in its own life history and its inherent properties of proliferation, differentiation and organization.

In figure 1 *A*, I believe it is apparent that progress in time is all that is required for the area of epidermal replacement to increase, for the dermis to become permeated with these cells, for local nutrition to be interfered with, for necrosis of the central part of the gross lesion to occur and for the clinical presence of cancer to become self evident.

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21. Stryker, G. V.: J. Missouri M. A. **30**:15, 1933.
22. Mekie, D. E. C.: Am. J. Cancer **16**:971, 1932.
23. Broders, A. C.: J. A. M. A. **74**:656 (March 6) 1920; Arch. Path. **2**:376 (Sept.) 1926.

EXPLANATION OF FIGURE 2

Fig. 2.—*A*, small squamous cell carcinoma, type I(b), from the nose of a woman aged 85 years. The lesion, present for eighteen months, was wartlike in gross appearance (× 26½). *B*, small squamous cell carcinoma, type I(b), from the finger-tip of a physician aged 41 years, with blue eyes, who handled radium during eighteen years. This lesion, a scaly, horny "keratosis" evolved in not more than four years and was becoming painful on pressure and slowly enlarging (× 23). *C*, small squamous cell carcinoma from the ear of a physician aged 70 years, with blue eyes and white hair. The multilayered epithelial surface is expanding and folding into the dermis, forming a wartlike rapidly growing lesion, an example of type I(b). It began as a "scaly spot" and has been recognized by the patient for only two months (× 26).

Figure 2

Type II (*b*).—In fast growing lesions of only moderate coherence the centrifugal spread is little before buckling occurs and the corium is invaded. Lateral and centrifugal spread is an inverse measure of activity: the most malignant lesions are of least area in reference to point of initial downgrowth. In carcinoma of this type the coherence of the cells is slight, and they spread into the dermis in narrow strands. Clinically, microscopically and theoretically they are more malignant than those of type I. The cells are different from normal in size, tinctorial reaction to stains and size of nucleus, and these features are apparent in the photomicrographs.

Type III.—The growth of a colony of progeny of an altered cell may be practically without coherence.

(*a*) If slow growing, the cells permeate the epidermis (figs. 3, 4 and 5), as in Bowen's [20] disease or Paget's [24] disease of the skin.

(*b*) If swiftly growing, the clumps of cells expand within the epidermis, soon bursting through the normal confines, as they have done in figure 6. Lesions such as these require only a short time to become obvious cancers. At their appearance they are merely tiny, pinkish, waxy intradermal lumps 1 or 2 mm. in diameter, usually possessing a thornlike central scale, which represents the minute region of complete replacement of epidermis by the neoplastic cells. Cells spread into the dermis in isolated units and clumps of small numbers. These correspond to Broders' most malignant class. In theory they should be—and in fact they are—most malignant, as judged by their readiness to metastasize.

SUMMARY OF TYPES OF EARLY EPIDERMAL NEOPLASIA

Characteristics of the types of initial cancerous growth in the epidermis may be summarized as follows: type I (a), strong coherence, slow rate of growth and development into horny and verrucous senile keratosis on the skin and leukoplakia on the mucous membrane; (b), strong coherence, swift rate of growth and development into squamous cell carcinoma which metastasizes late; type II (a), weak coherence (growth in a sheet), slow rate of growth and development into senile keratosis of slow progressiveness and erythroplakia on the mucous membranes; (b), weak coherence, swift rate of growth and development into senile keratosis that speedily becomes obvious and malignant cancer; type III (a), no coherence, slow rate of growth and development into Bowen's or Paget's carcinoma within the epidermis; (b) no coherence, swift rate of growth and development into malignant carcinoma, rapidly invasive and rapidly metastasizing.

There are intergradations of these processes. The classes designated by I (strong coherence), II (little coherence) and III (no coher-

24. Paget, J.: St. Barth. Hosp. Rep. **10**:87, 1874.

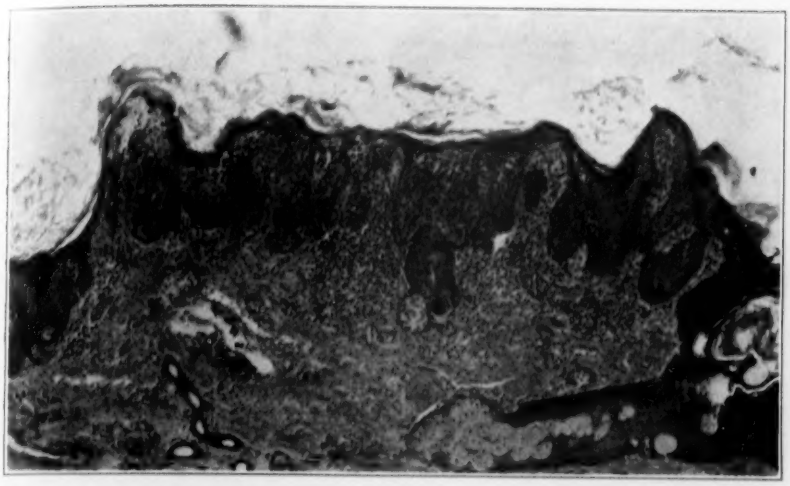

Fig. 3.—Intra-epidermal neoplasm of type III(a) The slowly proliferating cells permeate and bulge the epidermal papillae. The lesion was a scaling, flat-topped "keratosis" 2 mm. in diameter, on a woman's nose (× 50).

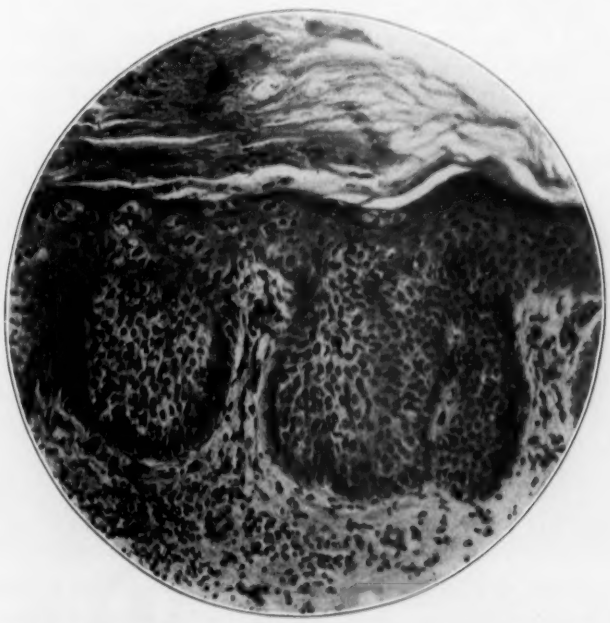

Fig. 4.—Intra-epidermal neoplasm (Bowen's disease) from a man's back. The neoplastic cells permeating the epithelium singly and in small groups, without coherence, make this an example of type III(a). The lesion was scaling and macular (× 120).

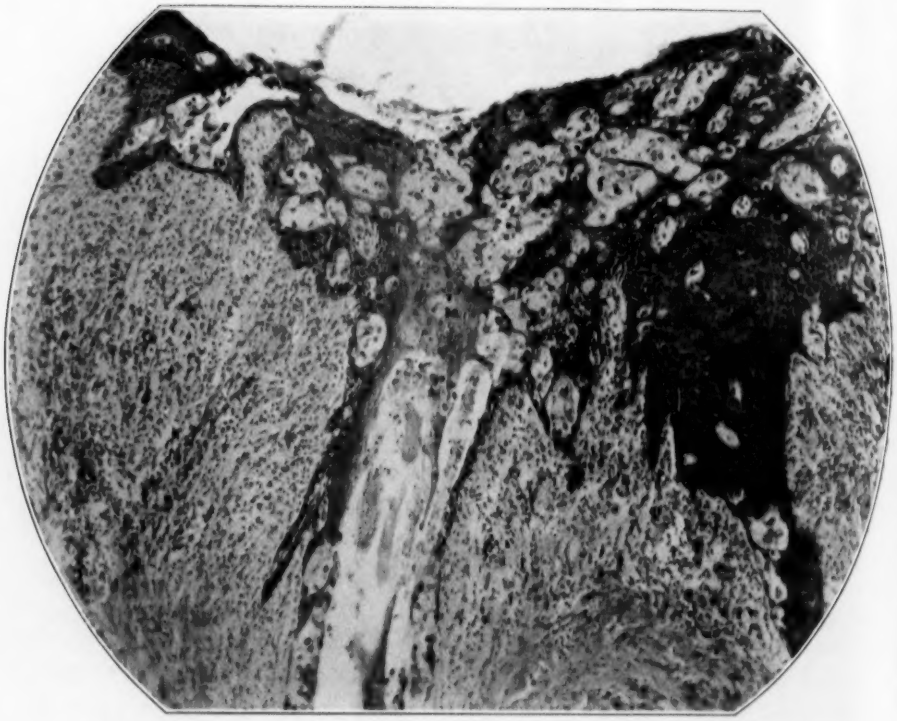

Fig. 5.—Section from Paget's disease of the nipple which proved fatal. The intra-epithelial carcinoma grew rapidly, showing hepatic metastases within six months of its first appearance. The cells were not coherent. The lesion was an example of type III(b) (× 120).

Fig. 6.—Speedy growth and lack of coherence (type III [b]) characterize the neoplastic process seen here, a pinkish papule with a central horny spicule from the face of a man aged 60 years. The lesion, which was intradermal, was an induration about 2 mm. in diameter, as judged by palpation. The central spicule, frequently cut when shaving, had been known to be present for about one year (× 44).

ence) and conditioned by (*a*) (slow rate of growth) and (*b*) (speedy rate of growth) form a complete set and accord with observation (table).

CONSIDERATIONS OF CELLULAR ACTIVITY

To consider the evidence that the cells of such lesions as I have described are different from normal it is necessary to disengage the mind from the belief that the differences must be striking and immediately evident to be real. Their speed of growth is a difference. The excess speed is proved by the mere fact of existence of a lesion, by the fact of scaling, by the fact of enlargement and progression and by the fact of buckling and warping of the cells en masse. Their color en masse is different from normal; the lesion is brown, of a hue distinct from that of a callus, which is an aggregation of cells that are not neoplastic. Their replacement of normal cells is a distinction in behavior. Their arranging themselves irregularly is another distinction in behavior. Their forming a scale that differs from the normal scale resulting from, say, sunburn, where epidermal reproduction is temporarily enhanced, is a distinction. The retention of nuclei in the scale is a difference, although this is seen in many lesions wherein no genetic alteration is postulated. The new cells are in general larger and have larger nuclei than their normal relatives. In preparations stained with hematoxylin and eosin there is usually a visible tinctorial difference, the neoplastic cells having more acidophilic cytoplasm.

MacCarty [25] has proved that the ratio of the size of the nucleolus to that of the nucleus is different, neoplastic cells having relatively large nucleoli. Regan, Page and MacCarty [26] reported larger and more numerous intranucleolar bodies in malignant cells. Fidler's [27] cytologic studies satisfied him that the malignant cell is a morphologic entity, recognizable in suitable preparations; irregular arrangement, absence of normal cohesion of cells with each other, irregularity of size, shape and staining qualities, coarseness of nuclear elements and large nucleoli are among observable differences from normal.

Lewis [28] expressed the belief that cancer cells are permanently altered cells, a new type or species, mutants according to some authors, changed by some sort of environmental influence; after alteration has been produced, continued action of the agency that produced it is no longer necessary. Vitamin A, present in the mitochondria of normal cells, was not found in the mitochondria of some tumor cells, despite

25. MacCarty, W. C., and Haumeder, E.: Am. J. Cancer **20**:403, 1934. MacCarty, W. C.: ibid. **26**:529, 1936; J. A. M. A. **107**:844 (Sept. 12) 1936.

26. Regan, J. F.; Page, R. C., and MacCarty, W. C.: Proc. Staff Meet., Mayo Clin. **12**:257 (April 28) 1937.

27. Fidler, H. K.: Am. J. Cancer **25**:772, 1935.

28. Lewis, W. H.: Proc. Staff Meet., Mayo Clin. **12**:250 (April 21) 1937.

its availability in normal amounts in the animals' livers.[28a] Schiller [29] has observed a chemical difference, which is not pathognomonic, in that neoplastic epithelial cells, lacking glycogen, do not stain with tincture of iodine as normal cells do. Schiller [29a] demonstrated the existence of a sharp transition from normal to abnormal epithelium in early carcinoma of the cervix uteri and remarked the resemblance of cervical lesions to those of the skin. The microscopic evidences of the distinctness of the two types of cells are apparent in my photomicrographs. Geschickter and Koehler [30] showed in their figure 6, as "precancerous change" in senile keratosis, the growth in a sheet such as I described as type II (a) (fig. 1, *A*).

Ludford [10] has reviewed the knowledge of chromosomal mechanisms pertinent to the theory of the origin of cancer in somatic mutation. Evans and Swezy [31] found in the human being twenty-three pairs of autosomes and the sex chromosomes x and y, the latter chromosome being a small granule. They were able to recognize these in somatic cells during mitosis. It is probable that the number of chromosomes in normal somatic cells is the same as that in the fertilized egg. In carcinoma of the jaw in a human being they found the normal number. Heiberg and Kemp,[32] confirmed by Levine,[33] found in human carcinoma the diploid (normal) number, and in some cells the tetraploid number, in irregular arrangement. Ludford [10] cited the counts of Painter, of Minouchi, of Hirschfeld and Klee-Rawidowicz and of Lewis and Lockwood, who found similar variations in the number of chromosomes in malignant cells, there being in the Jensen rat sarcoma tissue culture subdiploid, diploid, subtetraploid and polypoid numbers. Lambert [34] found the same abnormalities in the cells of rat sarcoma in vitro as in vivo. Winge's [35] graphs of counts in tar-induced tumors in mice showed two maxima, 38 and 68. Mottram [36] found an increase in the occurrence of nondisjunction in Drosophila when the female was treated with gamma radium radiation before fertilization or was exposed to carbon dioxide. Schairer,[37] having graphed curves of nuclear volume

28a. Goerner, A., and Goerner, M. M.: J. Biol. Chem. **123**:57, 1938.

29. Schiller, W.: Lancet **1**:1228 (May 30) 1936; Am. J. Surg. **26**:269, 1934.

29a. Schiller, W.: Surg., Gynec. & Obst. **56**:210, 1933; **66**:129, 1938.

30. Geschickter, C. F., and Koehler, H. P.: Am. J. Cancer **23**:804, 1935.

31. Evans, H. M., and Swezy, O.: The Chromosomes in Man: Sex and Somatic, Berkeley, Calif., University of California Press, 1929.

32. Heiberg, K. A., and Kemp, T.: Virchows Arch. f. path. Anat. **273**:693, 1929.

33. Levine, M.: J. Cancer Research **14**:400, 1930.

34. Lambert, R. A.: J. Exper. Med. **17**:499, 1913.

35. Winge, O.: Ztschr. f. Zellforsch. u. mikr. Anat. **10**:683 (June 6) 1930.

36. Mottram, J. C.: J. Exper. Biol. **7**:196 and 370, 1930.

37. Schairer, E.: Ztschr. f. Krebsforsch. **43**:1 (Nov. 18) 1935.

frequency of a number of tumors, decided that every cancer appears to be individual, with laws unto itself. It was Boveri,[38] working before 1914, who observed tripolar and tetrapolar mitoses in the eggs of the sea-urchin and expressed the hypothesis that a cancerous growth might originate in a somatic cell which, as a result of a preceding multipolar mitosis, had acquired a defective chromosomal mechanism. Not every cell with such a constitution would become malignant, he said, for some might be nonviable while others would exhibit minor aberrations; but the chromosome complex must be sufficiently complete to maintain life and must render the cell unresponsive to inhibition by its environment. Boveri's conception implied that cancer cells must have a different number of chromosomes from normal, but this has since been proved false. Dr. Michel Gerundo told me that Naegeli-Akerbloom attributed the first formulation of the concept of mutation in malignancy to his assistant, Hans R. Schinz, and that Lunghetti gave credit for its origin to Westenhoeffer (1907), Holmer (1907), Janekelevitch (1910) and Ries (1910). Toward the close of the nineteenth century Menetrier developed the idea that cancer is due to pathologic cellular selection and the development of new, autonomous cellular races, although the Frenchman did not use the word mutation, according to Gerundo. Whitman [39] in 1919 took issue with von Hansemann's [40] interpretation of the cellular peculiarities in cancer. Von Hansemann had seen unequal and multipolar mitoses, and he gave the term "prosoplasia" to that process by which normal embryonic cells become adult and "anaplasia" to the reverse process, a process of undifferentiation or redifferentiation. Ströbe [41] observed atypical cells in other than neoplastic conditions and considered them degenerative, an opinion currently shared by MacCarty, who found cancer cells undergoing proper mitotic processes. One must agree that strains of cells which persist for twenty or more years without alteration in their tumor-producing properties must have a stable reproductive process. My own observations of changes in ova in atresia folliculi in the albino rat lead me to believe that the fragmentation of a cell into bits that contain varying amounts of chromatin is a phenomenon of degeneration. Whitman [39] stated that the "new cell race" theory of Hauser,[42] the sug-

38. Boveri, T., and Kabitzsch, C.: Verhandl. d. phys.-med. Gesellsch. **35**:67, 1902. Boveri, T.: The Origin of Malignant Tumors, translated by M. Boveri, Baltimore, Williams & Wilkins Company, 1929.

39. Whitman, R. C.: J. Cancer Research **4**:181, 1919; **5**:155, 1920.

40. von Hansemann, D.: Virchows Arch. f. path. Anat. **119**:299, 1890.

41. Ströbe, cited by Whitman;[39] cited by von Hansemann;[40] Beitr. z. path. Anat. u. z. allg. Path. **11**:10, 1892.

42. Hauser, G.: Virchows Arch. f. path. Anat. **141**:485, 1895.

gestion of Butlin [43] that the "cancer cell is the cancer parasite" and the nuclear doubling hypothesis of Oertel [44] are variants of the von Hansemann theory. Von Hansemann considered the anaplastic process a gradual one carrying the cell in a new direction, an opinion I do not share.

INTRA-EPIDERMAL CARCINOMA

The evidence of existence of neoplasia limited to the epidermis is accepted by a great many authors,[45] including Fraser,[46] who write:

> From the pathologic point of view the cells in Bowen's lesion have already undergone the changes of malignant neoplasia, and for this reason the lesion should be classified as intraepidermal carcinoma, not as precancerous.

Hookey [47] said: "The microscopic picture of keratoma senilis suggests the possibility of further evolutionary changes of malignant character." Eller and Ryan [48] observed: "When a senile keratosis becomes verrucous, it is carcinoma." Satenstein,[49] after careful deliberation, stated: "The early stage of the majority of epitheliomas is intraepidermal in development."

THE HYPOTHESIS OF "PRECANCEROSIS"

"Precancerosis" is a name popularly applied to an assortment of lesions. Definitions of "precancerosis" are vague. Sulzberger and Satenstein [50] defined it thus: "The term precancerosis is a term which must be kept to designate conditions which, while not yet cancer, will, if untreated, practically invariably become cancer." Bloch's [51] careful review gave this definition: "We call precancerous those pathological changes in tissue which, without being cancer, show the tendency sooner or later to develop into an actual cancer." He called this a "clinical-statistical" definition and postulated its application on two conditions: (1) the determination with mathematical certainty of the probability that a certain type of lesion will become cancer and (2) the reaching

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43. Butlin, H.: Lancet **2**:1535, 1911.

44. Oertel, H.: New York M. J. **86**:14, 1907.

45. (*a*) Freudenthal, W.: Arch. f. Dermat. u. Syph. **152**:505, 1926. (*b*) Jadassohn, J.: Beitr. z. klin. Chir. **136**:345, 1926. (*c*) Borst: Verhandl. d. deutsch. path. Gesellsch. **7**:110, 1904. (*d*) Muir, R.: J. Path. & Bact. **30**:451, 1927; Brit. M. J. **1**:809 (April 18) 1936. (*e*) Inglis, K.: Paget's Disease of the Nipple and Its Relation to Surface Cancers and Precancerous States in General, London, Oxford University Press, 1936.

46. Fraser, J. F.: Arch. Dermat. & Syph. **18**:809 (Dec.) 1928.

47. Hookey, J. A.: Arch. Dermat. & Syph. **23**:946 (May) 1931.

48. Eller, J. J., and Ryan, V. J.: Arch. Dermat. & Syph. **22**:1043 (Dec.) 1930.

49. Satenstein, D. L.: Arch. Dermat. & Syph. **33**:48 (Jan.) 1936.

50. Sulzberger, M. B., and Satenstein, D. L.: Arch. Dermat. & Syph. **28**:798 (Dec.) 1933.

51. Bloch, B.: Cancer Rev. **7**:65, 1932.

of agreement on the percentage of instances in which that type of lesion must develop into cancer before one may be allowed to call it precancerous—that is, if 50 per cent of such lesions, for instance, do become cancer, all such lesions may rightfully be considered precancerous.

The concept remains unclear. Heimann [52] said:

> The term "precancerous dermatosis" has that alluring quality which captivates the imagination and courts acceptance until analysis reveals that it is inappropriate. At what point does precancerous lose its prefix? Is the problem one of medicine or etymology?

Error lies in the fact that Bloch's [51] definition groups together under the one name "lesion" individual and distinct lesions of which some may become cancer. When he says "the probability that a lesion will become cancer . . . ," he implies that many individual abnormalities are seen, recognized, followed and tabulated. I say this is improper classing of abnormalities that do not belong together into a single set. I say it makes no more sense than arriving statistically at the probability that a sore may be cancer by grouping all ulcers 1 inch (2.5 cm.) across and tabulating the proportion of possessors of such ulcers who die of them. After such a probability is expressed numerically, nothing significant is yet known about a particular ulcer. There is, a priori, a 50 per cent likelihood that I am female, but I am not. It is an error of indiscrimination between "lesion" used to describe a class abstractly and "lesion" in the sense of "this spot on this man at this time." Looseness of usage makes the whole structure illogical. There is no one on earth who could draw a line with a blue pencil around a hundred spots on fifty people and convince me that he had circled one hundred identical lesions. I know that I cannot. I make the same kind of complaint that Mottram [9] did when he pointed out that "previous studies of benign and malignant warts following tar on mice have been detailed studies of individual mice, not of individual warts." "Lesions" are individual; each is an entity unto itself, and each has a different and individual time of appearance, rate of progress, microscopic structure and future. Until each lesion has been subjected to microscopic examination, no one knows what its minute structure and cellular constitution are. If many lesions are removed, bottled in formaldehyde, prepared and examined, several will be seen to be similar, and several groups of similar ones can be sorted out. Further, if a number of lesions are allowed to evolve in time and some of them are observed to have become obvious cancer, then by implication several of them will not have become cancer. Therefore, if for no other reason, these were not the same as the others in the beginning.

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52. Heimann, W. J.: J. Cancer Research **1**:343, 1916.

There is irreconcilable inconsistency in the definition, resting on the facts that microscopic identification of a set of lesions kills them and that tabulation of evolutionary results is a tabulation concerning lesions neither adequately examined nor logically classed together. There is irremediable inconsistency in stating that "this is a set of lesions each like the other," when they are not examined but are allowed to grow, for after the lapse of time some have and some have not taken a particular course. As Heimann stated—and I agree with him whole-heartedly—"No one on earth is clairvoyant enough to select a given pigmented macule . . . and point with certainty to its epitheliomatous future." Either a lesion does become cancer or it does not. It is not eligible to statistical analysis. If it does become cancer, it must have been cancer; and if it is cancer, no one can say when it was not cancer. I believe that a lesion is the same thing throughout its existence and that it cannot properly change its name, in the biologic sense, merely because it changes its size. The acorn is Quercus just as is the oak tree; the fertilized ovum in the human uterus is Homo sapiens; the 1 mm. circular, scaling intra-epidermal macule is cancer as appropriately as the stinking ulcer that destroys the malar bone and orbit. I deny the mathematical consistency of the allegation of a 20 [52a] or a 25 [47] per cent probability that a keratosis may become cancer, which gains popularity by repetition but reveals failure to differentiate "case" meaning patient from "case" meaning a particular lesion. Hookey [47] merely reported that "a few lesions became malignant, but exact statistics are not available." Twenty-five per cent of those examined (selected) looked (not were) malignant. It is not possible to build a statistical definition of "precancerosis."

The definition of Sulzberger and Satenstein [50] is easily dealt with. They said that "precancerosis" is a term which "must be kept to designate conditions which, while not yet cancer, will, if untreated, practically invariably become cancer." I should request them to demonstrate one lesion that is not cancer and which does become cancer.

Novak,[53] writing of cancer of the cervix uteri, expressed the belief that the term "precancerosis" serves a useful purpose in keeping before the physician the idea of lesions precursory to actual cancer but clinically benign in themselves, so that their removal gives a measure of protection against cancer. He remarked the long pause between the intra-epithelial and the invasive phase of cancer in situ. He recognized the existence of carcinoma in situ at the edge of invasive cancer. This intra-epithelial spread at the edge of ulcerative carcinoma is, as I am sure he must have observed, actually part of the tumor. If it is not

52a. Montgomery, H.: Arch. Dermat. & Syph. **32**:218 (Aug.) 1935; Radiology **25**:8 (July) 1935.

53. Novak, E.: J. A. M. A. **108**:1145 (April 3) 1937.

destroyed along with the major portion of the tumor, recurrence will take place. I have in times past followed a carcinoma across the lower lip from side to side; the wound of destruction would heal, and recurrence at the edge of the scar would be seen after a few months had passed. Nowadays I blister off all "leukoplakia" surrounding the infiltrative lesion and avoid such recurrences. This leukoplakia is always sharply marginated. I have seen—and I am sure my experience is not unique—inadequately fulgurated "leukoplakia" followed by the prompt and startling development of vegetating carcinoma. How frequently this happens after the application of silver nitrate to "precancerosis"! How can a razor nick start a cancer of the face other than by introducing the cells of a tiny, inappreciable, apparently inconsequential "keratosis" into the dermis, where they promptly grow into readily appreciable carcinoma? Schubert [54] has described the development of Bowen's disease into squamous carcinoma as a result of trauma. I have observed two instances in which "keratoses" which I blistered off incompletely with the cautery recurred a year later as discoid indurated intradermal cancer, which was examined microscopically at a later date. Novak [53] apparently believes that there is gradual histologic transition from benignity to malignancy, a belief shared by many experienced observers, but I am convinced that this is not the fact. Recognition that "carcinoma in situ" adjacent to ulcerative lesions is part and parcel of them is conducive to cures otherwise not obtainable and is the reason for traditional wide excision. This is explicable much more satisfactorily—as are other facts in the development of cancer—by acceptance of the interpretations presented in this paper. Eichenberg [55] describes the spread of carcinoma of the cervix over the vaginal mucosa as a superficial eroding process. Bucher [56] recognized the early stage of cancer of the cervix as leukoplakic. Schmitz, McJunkin and Macaluso,[57] as well as Schmitz and Benjamin,[58] expressed agreement with this interpretation of carcinoma—that it begins as such in the epithelial layer, produces intra-epithelial disease and progresses (not changes) into intradermal cancer.

Erythroplasia, which has been reported [58a] and discussed at length since Queyrat's [59] description, is of such a nature. It is carcinoma

54. Schubert, M.: Dermat. Wchnschr. **100**:333 (March 23) 1935.

55. Eichenberg, H. E.: Ztschr. f. Geburtsh. u. Gynäk. **111**:243, 1935.

56. Bucher, A.: Schweiz. med. Wchnschr. **66**:30 (Jan. 11) 1936.

57. Schmitz, H.; McJunkin, F. A., and Macaluso, M. A.: Am. J. Obst. & Gynec. **27**:336, 1934.

58. Schmitz, H., and Benjamin, E. L.: J. A. M. A. **103**:808 (Sept. 15) 1934.

58a. Kolb, E.: Dermat. Wchnschr. **96**:96 (Jan. 21) 1933. Stiles, F., Jr.: Arch. Dermat. & Syph. **30**:647 (Nov.) 1934. Irgang, S., and Alexander, E. R.: ibid. **34**:247 (Aug.) 1936. Touraine, A., and Solente, G.: Presse méd. **44**:1830 (Nov. 14) 1936. Sulzberger and Satenstein.[50]

59. Queyrat: Bull. Soc. franç. de dermat. et syph. **22**:378, 1911.

limited for a time to the surface layer, as Mekie,[22] describing its "raw beef" appearance, seemed to be aware. It is not invariably mucosal, for I, as well as Freund,[60] have seen "senile keratoses" of the same structure.

Somerford[61] observed that in occupational cancer the lesions first observed seem to be pimples or warts but are actually initial cancerous lesions, not "precanceroses." Lindberg's[62] investigation of forty-two cases of primary cancer of the lung showed that in fifteen cases of the squamous cell type the bronchi bore several lesions exactly analogous to the "precanceroses" seen on the faces of farmers with one or several carcinomas and other scaly patches. Atypical nuclei were present in these minor bronchial lesions, just as they are in senile keratoses. As Mottram[9] insisted, in accounting for the origin of cancer one must recognize the occurrence, in a single series, of both benign and malignant tumors. It is exactly this difficulty that makes the separation of the spontaneous human lesions under discussion not susceptible of division into two separate categories, "precanceroses" and cancers, or senile keratoses and cancers. These lesions are manifestations of one kind of alteration. The theory of mutation crosses this chasm by accounting for all the lesions as neoplastic, some being composed of more rapidly proliferating neoplastic cells than others.

Some who have read such concepts of mine as have been published hitherto[63] have objected to my contention that the process is continuous, from the initial cell that originates a particular cancer, through the stages by others called "precanceroses" to obvious cancer. I believe this process to be continuous, with no actual alteration in the type of cell. The size of a lesion is not a criterion of whether it is cancer. A solitary cell of malignant melanoma may reach the liver, proliferate and result in an orange-sized mass of tumor. The one cell is therefore as satisfactory a cancer from every standpoint (except that of visibility to the unaided eye) as is the half-pound lump that it engenders.

Some critics have observed that the quantitative growth of a lesion seems not to be uniform. They would say the earliest lesion that appears in the skin is 2 or 3 mm. in diameter, that it seems to remain stationary for many months before it suddenly takes on active growth and develops into cancer and that during this stationary period it is "precancerosis." I would point out that it requires a considerable period for the progeny of a single altered cell to become a visible

60. Freund, H.: Arch. f. Dermat. u. Syph. **167**:401, 1933.

61. Somerford, A. R.: Brit. M. J. **1**:1305 (June 29) 1935.

62. Lindberg, K.: Arb. a. d. path. Inst. d. Univ. Helsingfors **9**:1, 1935.

63. Sutton, R. L., Jr.: J. Missouri M. A. **32**:224, 1935; J. Oklahoma M. A. **28**:364, 1935; South. M. J. **29**:235, 1936; J. Kansas M. Soc. **28**:97, 1937.

colony. If there must occur replacement of epidermis over an area 1 or 2 mm. in diameter before the colony becomes visible, then about 1,000,000 cells must come into existence. (A circle 2 mm. in diameter has an area of about 3,000,000 square microns. By allowing 30 square microns for a basal cell and 10 layers of cells for thickness, one arrives at the result, 1,000,000 cells.[63a]) If mitosis occurs in each new cell twice a day, in contrast to the normal rate of once a day, then ten days would be required. If the ratio were 1.1 to 1 instead of 2 to 1, the time required would be about two hundred days. Having become visible, the lesion is nevertheless limited to the epidermis. It forms a scale; the scale falls off, and thereby the major portion of the colony is lost (Mottram's "wastage due to keratinization"). As the scale forms and reforms, the colony slowly comes to invade the dermis by the warping previously described. Then, when the cell divides, each daughter cell is in a favorable situation. Before the dermis was penetrated, one of the two daughter cells was closer to the exterior and was soon to be lost in the scale; now, however, the cells are surrounded by soil in which they can grow, and a period of development during which progress is clinically much more rapid is entered. This apparently increased rate of growth, however, is not a true measure of the rate of proliferation of the neoplastic cells. They may have been reproducing at a uniform rate from the moment of the coming into existence of the first altered cell from which they are descended; yet the loss in the form of scale has maintained the colony at a small and nearly uniform size until the dermis is entered. Thus, the malignancy, as far as rate of mitosis and potentiality for doing harm are concerned, has been present undiminished during the progress from its inception as a single cell until the colony has invaded, ulcerated and even killed its host. When the dermis is invaded, the rate of growth may appear to have increased by leaps and bounds, and the observer may be tempted to say that the degree of malignancy has altered from nil to much; yet the truth is, in my opinion, that no such alteration has occurred and that the period in the colony's existence called "precancerosis" is in fact misinterpreted by the observer, who fails to recognize that scaling alone suffices to account for the apparently stationary stage. The scaling macule, the "precancerosis" and the cancer evolved from it are the same thing. The lesion was, is and will continue to be the same cancer, and its degree of malignancy has not altered in the process.

63a. Compare Mottram, J. C.: J. Path. & Bact. **40**:407, 1935; this explanation of the latent period is more satisfactory, I believe, than a hypothesis involving "allergy," suggested by F. Wise and M. B. Sulzberger (Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc., 1937, p. 280).

Why do "precanceroses" in epithelium such as that of the skin, the mouth and the bronchi occur always as scaling patches? Is it not because the reproductive products of altered cells are lost by scaling, while the progeny are nonproductive because of their distance from nutriment? Daughter cells have not equally favorable circumstances for proliferation when they are pushed toward the surface. Within tissue instead of on tissue proliferation would lead to the formation of spheroid tumors, not scaling patches. Expansion of an analogous area of abnormal epithelium in intestine or bladder produces a papilloma with a surface vastly larger than the surface it replaces. When a benign melanoma or simple nevus is propounded as an example of "precancerosis," I would point out that abnormal tissue is tissue in which mutation is likely to occur. Before it has, cancer is not present; when cancer appears, it does so abruptly. Lockhart-Mummery [64] described investigations showing that malignancy which supervenes on a benign tumor does in fact begin in a small part thereof. Mottram's [9] experiments showed that parts of a single tar-induced lesion may differ in malignancy, as proved by transplantation.

There is a latent period between the application of the carcinogenic agent and the development of experimental cancer which requires consideration. Mottram,[9] using tar on mice, found that lesions first became visible from one hundred to one hundred and fifty days after the applications were started. They were a millimeter or more in diameter when first seen. Those which appeared first were not necessarily the most malignant. There was great variation in the rate of growth. Those in which growth suddenly speeded up were malignant, as tested by transplantation. Part of a solitary induced tumor might prove malignant while the remainder did not. I believe the inability to observe lesions before one hundred days had elapsed is to be explained by the fact that until the epidermis was entirely replaced by the progeny of the altered cell no visible lesion would exist, and such replacement requires time. It is easily possible that the microscope might have revealed otherwise invisible lesions before one hundred days had elapsed, but that was not determined, so far as the report stated.[65] In sections of lesions excised from xerodermatous subjects, I have seen, separated from the lesion for which the section was made, isolated proliferations that strongly suggest commencing lesions of submicroscopic dimensions, apparently

64. Lockhart-Mummery, J. P.: The Origin of Cancer, London, J. & A. Churchill, Ltd., 1934, p. 116.

65. Such investigations were under way when I visited the Laboratory of the Imperial Cancer Research Fund in July 1937. Dr. W. E. Gye has a benzpyrine derivative of which a single application frequently initiates carcinoma of the skin of mice.

unrelated to the principal lesion. These are described, but not interpreted, in the usual histologic studies of xeroderma pigmentosum. It would require great good fortune to find a lesion composed of fewer than several hundred cells in an area of skin 1 cm. square.

Gehrmann [66] has written about cancer of the bladder among handlers of dyes. The lesions form, just as do tar-induced tumors of the skin, a series grading from slowly growing villous papilloma to highly anaplastic carcinoma. Removal of the subject from further exposure to the dye does not lessen his liability to further development of tumors. An average of twelve years following exposure is required for vesicular symptoms to develop. Some handlers get cancer; most of them do not. Each human being's tissues have a definite inherent capacity for response by atypical growth to dye metabolites which is aptly analogous to the susceptibility demonstrated in mice by Slye.[67] Some persons require much less than twelve years to manifest disease. The interval is that which is required for a colony of progeny of an altered cell to make its presence known.

If there were not an interval between the application of the carcinogen and the development of carcinoma (this is not the case in sarcomas transmissible by cell-free filtrates, which are not satisfactorily accounted for by the theory of mutation), then one might believe that many cells had been immediately altered rather than that one altered cell required time to produce a visible colony. It is this interval which differentiates cancerous initiation from homeogenic induction in embryologic experiments.[68] Needham [69] pointed out the similarity of carcinogenesis to chemical evocation of normal growth, organizers having been shown to be sterol substances related to hormones and carcinogens. But the organizer evokes normal differentiation at once, and the carcinogen evokes abnormal organization seemingly after a time. As Cramer [70] said, "Whatever it is that drives on malignant cells to their uncontrolled growth resides within the cells," once the initial alteration has been brought about. Many interrelationships between carcinogenesis and homeogenic induction will doubtless be proved, but organizers [70a] evoke normal organization even in unusual locations, while the result of carcinogenesis is disorganizing.

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66. Gehrmann, G. H.: J. A. M. A. **107**:1437 (Oct. 31) 1936.

67. Slye, M.: J. A. M. A. **86**:1599 (May 22) 1926.

68. Huxley, J. S., and De Beer, G. R.: Elements of Experimental Embryology, London, Cambridge University Press, 1934, p. 148.

69. Needham, J.: Brit. M. J. **2**:701 (Oct. 10) 1936; Order and Life, New Haven, Yale University Press, 1936.

70. Cramer, W.: Brit. M. J. **2**:781 (Oct. 17) 1936.

70a. Basic understanding of organization is as yet not extensive (Weiss, P.: Physiol. Rev. **15**:639, 1935).

I wish here to correct an error in the abstract of my article of 1934 on early cutaneous carcinoma.[71] I described small lesions of such structure that the microscopist would believe that if not interrupted they would become obvious cancer. I have been erroneously quoted, on page 314, as saying that "It is not reasonable to believe that such lesions are in fact early carcinomas." The "not" in that sentence does not belong there. Its being there spoils the entire argument, which was designed to convey the thought, that if a lesion under magnification looks as if further proliferation would produce the structure of obvious carcinoma, then in fact the lesion probably is early carcinoma.

Wise and Sulzberger [71] in editorial comment distinguished a practical clinical from a theoretical laboratory aspect of the controversy. Such a distinction, which they made for the benefit of the practitioner, is suitable for those to whom a microscope is a mystery, to whom cells are something Virchow was once known to have been excited about or to whom malaria is a swamp fever due to miasms. Contrary to those authors' opinion, a patch of leukoplakia which is undergoing hypertrophy, roughening and ulceration is cancer; the early stage of Bowen's disease is cancer, just as the late stage of it is; erythroplakia of Queyrat is superficial cancer; a roentgen burn is not cancer, until cancer makes its appearance. "Precancerosis" is, from the clinician's point of view, a confusing makeshift to cover ignorance of small anomalies, an ignorance which is more readily dispelled by the use of the lens than by "forgetting the microscope for a while." I am among the first to admit that knowing what is cancer and what is not is likely to be difficult in a particular case; I am delighted with the emphasis on destroying a lesion whether its harmful potency be known or only suspected, and meanwhile I am intensely interested in learning what can be learned of the intimate nature of small lesions rather than, alternatively, sticking my head into the sand.

The desirability of keeping the term "precancerosis" seems meager to me. Bloch [51] considered the concept of practical importance because "the knowledge of precancerosis gives us the only means of practicing effective prophylaxis of cancer." It is my contention that effective prophylaxis is intimately dependent on knowing what is cancer and what is not, rather than on knowing what might be cancer while hoping for the best.

In summary, "precancerosis" is a hypothesis, not a lesion. "Precancerosis" is anything the user of the term may define it to be, whereas definition will not alter a lesion. "Precancerosis" is anything in which

71. Wise, F., and Sulzberger, M. B.: Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc., 1935, p. 314.

neoplastic alteration may take place; any mammal as a whole [71a] is a "precancerosis." The concept can accord with current knowledge of cancer only in the blanket sense of indicating any condition in which cancer may supervene. It is as unscientific a term as "rheumatism" and covers as many different things. It is both useless and confusing for biologic comprehension.

THE THEORY OF MUTATION

The theory of mutation in the origin of cancer is a theory in which it is postulated that neoplasia is the result of genetic alteration in proliferating somatic cells. The alteration may be spontaneous or induced. The progeny of the altered cell constitute the parenchyma of the tumor. The theory implies that other theories are erroneous, including the Cohnheim [72] hypothesis that cancer arises in a misplaced embryonic cell and hypotheses of infectious, virous and traumatic origin. It implies that a cell may be so altered genetically that it ceases to be a part of the united and cooperative collection of metazoan cells which constitutes an organized animal and becomes analogous to a protozoan parasite, i. e., that a cell may genetically lose its capacity for organization as a part of a whole.

Whitman,[39] in suggesting the theory of somatic mutation, apparently unaware of Boveri's [38] work, insisted that the alteration from normal to neoplastic is immediate, not gradual. His hypothesis was suggested by Hoffman's [73] studies, which indicated that cancer is rare in aboriginal stocks. Whitman adduced corroborative evidence that mongrelized plants and animals do not breed true. He gave Prof. T. D. Cockerell, his superior at the University of Colorado, a share of the credit for the conception of somatic mutation as the origin of cancer.

With this background it is a little surprising to read Lockhart-Mummery's [64] sentence, "It was in March 1932, at a meeting of the Harley Society, that I first put forward the theory of gene mutation of somatic cells as an explanation of the genesis of tumors." Ludford's [10] paper of 1930, which he quoted with familiarity, is as good a statement of the theory as his own, which is more popular in its form of presentation.

71a. The capacity for malignancy as a universal character of cells was discussed by W. F. Dunning, M. R. Curtis and F. D. Bullock (Am. J. Cancer **28**:681 (Dec.) 1936.

72. Cohnheim, J.: Vorlesungen über allgemeine Pathologie, Berlin, A. Hirschwald, 1877.

73. Hoffman, F. L.: The Mortality from Cancer Throughout the World, Newark, N. J., Prudential Press, 1915.

EVIDENCE OF SOMATIC MUTATION

The possibility of somatic mutation must be looked into. Mutation of germ cells has been studied with great diligence and fruitfulness by geneticists since the time of de Vries.[74] Practically all evidence points to alteration in distribution, separation, combination or constitution of chromosomes as the basic factor in mutation, and the mutation occurs at the time of mitotic production of germ cells, before union of male and female elements. There are numerous observations and experimental studies which show that the same process may involve proliferating somatic cells. Dunning [75] reported that roentgen treatment of the parasitic wasp, Hebrobracon juglandis (Ashmead), produced with increasing doses a progressively increasing incidence of somatic abnormalities, diminished fertility and decreased visibility. Demerec [76] found that roentgen rays increase the rate of incidence of genetic changes, the effect varying with the dosage. Metz [77] observed loss of genes in the cells of the salivary glands of Drosophila. Jones [78] stated that mosaics involving the same genes vary markedly in frequency in different stocks, that they may result without the action of a known external agency and that their frequency is increased by agents which cause an increased frequency of neoplasms. The effect of roentgen rays, of radium, of hormones and of other agents in bringing about unregulated growths, Jones said, seems conclusively to be due in some way to their action upon the chromosomes, resulting in the loss of parts or of whole chromosomes." Timoféeff-Ressovsky [79] observed that the quantity of roentgen radiation, not the way it is given or its wavelength, determines the effect upon mutation in Drosophila.

Muller [80] in 1928 reviewed the subject of mutation caused by roentgen rays in Drosophila. Lethal mutations occurred in a proportion of 1 to 947 in the controls and of 88 to 758 in the treated flies. In another series there were greater effects from greater doses. Graphs showed the effects of roentgen rays to be heaped at the same chromosomal regions as spontaneous mutations are.[80a] The mutants bred true. He concluded that practically all changes in the genes are losses and that

74. de Vries, H.: The Mutation Theory, translated by J. B. Farmer and A. D. Darbishire, Chicago, Open Court Publishing Co., 1909.

75. Dunning, W. F.: Genetics **16**:505, 1931.

76. Demerec, M.: Proc. Nat. Acad. Sc. **20**:28, 1934.

77. Metz, C. W.: Proc. Nat. Acad. Sc. **20**:617, 1934.

78. Jones, D. F.: Proc. Nat. Acad. Sc. **21**:90, 1935.

79. Timoféeff-Ressovsky, N. W.: Strahlentherapie **49**:463, 1934.

80. Muller, H. J.: Proc. Nat. Acad. Sc. **14**:714, 1928.

80a. The natural rate of mutation in Drosophila is perhaps a hundred times as great as in the human being, stated C. H. Waddington (Brit. M. J. **1**:642, 1938).

only rare changes due to roentgen rays are not losses. He found translocations to be as common as mutations and stated that roentgen rays may cause both mutation of the genes and reorganization of the chromosomes. He observed that immature animals can be caused to become mosaic adults with patches of mutant tissue derived from mutant larval somatic cells. Muller and Prokofyeva [81] in 1935 wrote that some changes in the genes which once were thought to be mutations are due to deficiency or change of position. Mutations without any visible differences in the region of the chromosomes where they reside are perhaps the result of physical or chemical change in the gene. Changes of this kind affect many growth-regulating processes in animals and plants. Most deficiencies of the genes are lethal, but viable deficiencies have been obtained. The authors concluded from evidence from several sources that the actual magnitude of a gene is of the order of one protein molecule, that in Drosophila the total number of genes is from 5,000 to 10,000 and that differences of the order of the size of one gene are visible in the salivary chromosomes. Changes simulating mutations accompany rearrangements of the genes and are due to the localized influence of propinquous genes on one another, an influence which fades with distance.

Patterson [82] reviewed the results obtained by Muller [80] in 1928 in the application of roentgen radiation to the germ cells of Drosophila. Patterson treated flies in their multicellular stages, as eggs and as larvae, with the object of obtaining somatic mutations. He got several kinds of somatic alteration, none of which proved inheritable, this fact being positive evidence that the change was in somatic cells. The changes were principally in the form of irregular patches of color of the eye, the size of which varied inversely with the age at the time of irradiation. Treatment during the larval stage produced these changes; treatment at the pupal stage did not.

Stadler,[83] experimenting with the effects of roentgen irradiation on maize, found the percentage of mosaics from treated pollen to be twenty times as great as that from the untreated substance. In 1928 Stadler [84] treated the germinating seeds of barley and found that all induced mutations were somatic, affecting only part of the plant. While most of the variations obtained had been previously described as of natural occurrence, some were new.

Stark [3] observed a melanotic tumor that appeared as a mutant in Drosophila. It was sex linked, occurring in half of the male larvae, and

81. Muller, H. J., and Prokofyeva, A. A.: Proc. Nat. Acad. Sc. **21**:16, 1935.
82. Patterson, J. T.: Science **68**:41, 1928; J. Exper. Zoöl. **53**:327, 1929.
83. Stadler, L. J.: Proc. Nat. Acad. Sc. **14**:69, 1928.
84. Stadler, L. J.: Science **68**:186, 1928.

killed the flies in the larval stage. Death seemed mechanical. Later the author [85] found another pigmented tumor which was not sex linked and not necessarily lethal.

SOMATIC MUTATION IN EPIDERMAL NEOPLASIA

Thus it is seen that adequate experimental and observational evidence exists to satisfy one that somatic mutation may and does occur. Any somatic cells which are normally proliferative throughout the lifetime of the soma of which they are a part are incompletely differentiated; they are ancestral cells that undergo mitosis time after time, and they may, a priori, be expected occasionally to manifest genetic alteration. The fibrotic dermis is composed of cells which undergo mitosis rarely, and primary tumors of the dermis are rare. The epithelium of the epidermis continually undergoes mitosis, the number of reproductive events in an adult's skin approaching 60,000,000,000 daily, and primary tumors of these cells are common. The activity of the epidermis is easily seen in the growth of hair; tumors composed of cells closely resembling those of the hair follicles are common. Fat "secretion" actually consists of fatty degeneration of glandular cells and their replacement by proliferation. On the face, where fat secretion is most active, tumors composed of cells resembling those of the active layer of fat glands are common. The mammary glands similarly secrete by proliferation and alteration of epithelial cells; mammary tumors are common. I believe it is safe to say that where mitosis is most frequent, neoplasia is most frequent; that this relationship is one of cause and effect, and that neoplasia is the direct result of mutant cellular reproduction.

I have adduced evidence that squamous carcinoma of the skin begins as a minute lesion composed of few cells. These cells are different from neighboring normal ones. They are, among themselves, of a single kind, although they may undergo degeneration analogous to the generation of normal cells. They grow faster than normal ones grow. Their proliferation results in the formation of lesions which may be benign or malignant, dependent largely on their rate of reproduction. Having lost the faculty of organization as a part of a whole, their malignancy, or rate of doing harm, is directly related to their rate of proliferation.

Since it is impossible to obtain material for microscopic examination of lesions composed of many fewer cells than those I have demonstrated, and since a solitary cancer cell would not be recognized if seen, recognition (not existence) being dependent on the relation of groups

85. Stark, M. B.: Proc. Soc. Exper. Biol. & Med. **17**:51, 1919. Stark, M. B., and Bridges, C. B.: Genetics **11**:249, 1926.

of cells and their behavior rather than on the morphologic picture of the individual cell, I admit it is an assumption to say that the origin of a group is one cell. Examining the reasonableness of this assumption, one notes that the group spreads centrifugally both as a clinical lesion and from the microscopist's point of view.[85a] When it was smaller than those I have photographed, it must have been composed of fewer cells, located in what is now the center of the lesion. These are more likely to have come from one cell than from several, for the probability is slight that several should alter in the same way and give rise to progeny which are indistinguishable.

Furth, Kahn and Breedis [85b] claimed to have transferred mouse leukemia by the transference of one leukemia cell.

FILTRABLE VIRUSES IN CARCINOGENESIS

I have given reasons for believing cancer is a cellular disease, and I must limit this statement to carcinoma, for the Rous sarcoma, as well as others of fowls, are specifically transmissible by cell-free filtrates. How this can be so is unknown. It is not impossible that the tumor in its growth produces locally a carcinogenic substance which is transferred by the injection of the filtrate, as Murphy [86] has suggested. Cramer and Horning [87] have confirmed Lacassagne's observation that a carcinogenic agent, estrogen, applied to the skin of mice will evoke mammary cancer even in male mice. Thus an agent that causes cellular alteration may move within a host and affect a specific group of specifically vulnerable cells. Selbie [88] reported inducing tumors by the injection of cell-free filtrates of benign rabbit papilloma, but the virus disappeared if the tumor changed to a malignant one. That carcinoma should develop in Shope and Hurst's [89] rabbits with virus-induced papilloma, as demonstrated by Rous and Beard,[90] is not inconsistent with the theory of mutation. Rous, Kidd and Beard [90a] described the phenomenon in detail and observed that traumatic operations on these carcinomas produced metastases in the lung by cellular embolism. Bittmann [90b] showed that

85a. This directly contradicts the apparent meaning of L. Szodoray (Arch. Dermat. & Syph. **36**:552 [Sept.] 1937).

85b. Furth, J.; Kahn, M. C., and Breedis, C.: Am. J. Cancer **31**:276 (Feb.) 1937.

86. Murphy, J. B.: Proc. Staff Meet., Mayo Clin. **11**:789, 1936.

87. Cramer, W., and Horning, E. S.: Abstracted, J. A. M. A. **108**:1565 (May 1) 1937.

88. Selbie: Abstracted, J. A. M. A. **108**:1565 (May 1) 1937.

89. Shope, R. E., and Hurst, E. W.: J. Exper. Med. **58**:607, 1933.

90. Rous, P., and Beard, J. W.: Proc. Soc. Exper. Biol. & Med. **32**:578, 1935; J. Exper. Med. **62**:523, 1935.

90a. Rous, P.; Kidd, J. G., and Beard, J. W.: J. Exper. Med. **64**:385 and 401, 1936.

90b. Bittmann, O.: Ztschr. f. Krebsforsch. **22**:278 (April) 1925.

appropriate tarring of rabbits' ears might lead to the production of carcinoma within a few weeks. Ordinarily, however, tarring does not result in cancer in less than four months, but, according to Gye,[90c] if injection of Shope's papilloma virus accompanies the tarring of the ears, carcinogenesis within three weeks will result, both at the site of papilloma formation and on tarred areas devoid of papillomas, but not on areas that have not been tarred. Rous and Beard [90d] have remarked the similarities of carcinomas and warts induced by tar and by Shope virus and suggested that tar tumors may be due to virus dependent for pathogenicity on derangements of tissue such as tar produces. Gye [90c] has turned toward a belief that the change from hyperplasia to malignancy may be the result of the entry of a virus. He stated that the theory of mutation is verbal and is "unprofitable for further consideration." It seems to me that all that has been proved is that two carcinogenic agents operating simultaneously are more efficient than one, as Mottram [90e] showed. Foulds [90f] demonstrated that an antibody capable of neutralizing Rous sarcoma 1 is produced in the serum of a rabbit when tissue from a tumor induced by dibenzanthracene is injected into the rabbit. Shope [89] observed the existence of immunity to the papilloma virus on the part of rabbits infected with it and that their serum neutralized the virus. This is a different thing from the observation of Foulds,[90f] the implications of which appear to be incompatible with the theory of mutation. Perhaps, as Foulds suggested, an intracellular virus-protoplasm complex is formed, and filtrability depends on dissociation of this complex. There is no reason for believing that such a virus-protoplasm complex may not be an addition to, or detraction from, a gene or group of genes by chemical or immunologic association, so that the gene, for genetic purposes, is lost. The specificity for tissue of virus carcinogenesis favors rather than detracts from such a hypothesis. The variation of types of cell in tumors produced by one virus, as Rous [91] noted, may be so explained.

It must be admitted that the existence of virus-induced neoplasia is the most potent argument against the theory of mutation. But certainly the weaknesses of the virus theory of the cause of all neoplasia are almost hopelessly unsurmountable. Each virus is specific for the type of neoplasm it produces. Multiplicity of types of tumors derived from one tissue is unaccounted for by the virus theory. Mutation accounts for multiplicity of types of cells and their resemblance to normal

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90c. Gye, E.: Brit. M. J. **1**:551 (March 12) 1938.

90d. Rous, P., and Beard, J. W.: Proc. Soc. Exper. Biol. & Med. **33**:358 (Dec.) 1935.

90e. Mottram, J. C.: Am. J. Cancer **32**:76, 1938.

90f. Foulds, L.: Am. J. Cancer **31**:404 (Nov.) 1937.

91. Rous, P.: Am. J. Cancer **28**:233, 1936.

tissues as does no other theory, in the opinion of McGowan.[91a] I concur in this belief. Rous [91] has pointed out, however, that in the failure to demonstrate an extrinsic cause for tumors in general technical difficulty must not be mistaken for biologic principle. A malignant growth in identical twins may mean, he said, that the soil and the contributory circumstances are right, so that the virus is effective; the experimental induction of cancer where it does not occur normally may indicate that some decisive conditioning is made present in that area. Rous [91] called tumor cells "sick" cells, for when transplanted the most malignant die most easily, while the slow-growing tumors are hardier; Lewis, he said, has remarked that tumor cells are "notoriously afflicted with chromosome troubles." The argument thus confirms either hypothesis. Rous expressed the belief that cancer does not spring full blown from normal cells but develops as a result of gradual changes induced by carcinogens; this belief I do not share.

THE ORIGIN OF CARCINOMA IN SOMATIC MUTATION

Since the soma is a colony of cells derived from one cell, it is possible that the whole strain may possess an inherent potentiality for mutational instability. Wright and Eaton,[92] studying color patterns of 40,000 guinea pigs of known heredity, showed that mutant variations occurred with disproportionate frequency in one family. Little [93] observed a hereditary tendency toward germinal instability. Strong,[94] studying a transferable mouse neoplasm, showed that one strain of the tumor would grow in all mice, while others would grow in only some. Selbie [88] confirmed the finding of hereditary natural resistance to transplantation of two mouse tumors. Strong [94] observed that the cell is the unit of malignant tissue, as of normal; that inoculation with malignant tissue is a transplantation and not an infection; that few of the transferred cells live in the new host, and that uniform behavior of a tumor implies a relatively stable mechanism for its perpetuation. He expressed the opinion that somatic mutation may occur in a tumor cell and result in changed physiologic activity of the tumor tissue.

Mutants constitute a strain in which further mutation is often more frequent than in the parent strain. Slye's [67] evidence of the inheritability of the tendency to cancer has been cited. In 19,000 mice she [95] found twenty-eight tumors of the testis, and all these occurred in a single strain of mice and its hybridizations.

91a. McGowan, J. P.: Brit. M. J. **1**:698 (March 26) 1938.
92. Wright, S., and Eaton, O. N.: Genetics **11**:333, 1926.
93. Little, C. C.: Am. Naturalist **50**:335, 1916.
94. Strong, L. C.: Genetics **10**:294, 1926.
95. Slye, M.; Holmes, H. R., and Wells, H. F.: J. Cancer Research **4**:207, 1919.

If mutation may occur in germ cells, it may occur in somatic cells as well, for in proliferating tissues any cell is a "germ cell" so far as its progeny are concerned and an ancestral cell when looked back on after the lapse of time. If further mutation within a benign lesion should produce a malignant lesion, the benign lesion could be looked on as "precancerosis" in the sense of its being a lesion in which such alteration might occur. Whether a large or a small proportion of cancers of the skin result from such a procession of events—mutation following on mutation—is not within my knowledge. If the concept of cancer arising in mutation is acceptable, the concept of precancerosis as a lesion in which mutation is likely to occur may be approved.

A mutant, having once come into existence, breeds true. The fact that metastases breed true is consonant. If some 60,000,000,000 mitoses occur in the skin daily, would it not be surprising if some of them were not defective? How might the erroneous mitosis become visible? Why not in the form of colonies of cells that en masse assume the appearance of circular, brown, expanding, scaly spots on the skin? If mutation is dependent on chance alone, the mutations would occur in proportion to the total number of mitoses that have taken place in the soma. The maximum incidence would be in advanced age, but occasional mutations would occur at early ages. Frank [96] recorded a case in which carcinoma of the tongue was present at birth!

Need a mutant be astonishingly different from normal to be really a mutant? No, for an albino differs only slightly from normal morphologically and in behavior. The cells of benign keratosis differ radically from their fellows in behavior if not in individual appearance.

If the lesions I speak of are mutations, what implications become apparent? The cells may be assumed to have lost something. If treated with roentgen rays, they promptly lose more. Hence radiosensitivity may be expected, and experience proves this to exist. Mottram [90e] found that by painting mice with benzpyrene and simultaneously treating them with radium he obtained tumors with an amount of painting otherwise insufficient for carcinogenesis. Why does roentgen irradiation not cause sarcoma of the skin as commonly as carcinoma? Because the cell is vulnerable only when mitosis is taking place, and this is not happening frequently in the dermis. Sarcoma has been known to result from irradiation.[97]

Will separation of the colony from the host suffice to cure? A priori, I should say yes, and experience is corroborative. One cannot excise a chancre and cure syphilis; but one may excise a carcinoma of

96. Frank, L. W.; Enfield, C. D., and Miller, A. J.: Am. J. Cancer **26**:775, 1936.

97. Alius, H. J.: Beitr. z. klin. Chir. **143**:567, 1928.

the skin, preferably by using a hot iron, and if the cells are all removed, the patient gets well and stays well. This fact is one of the approximate medical certainties. I feel much more sure of the result of amputation of local cutaneous cancer by cautery than of that of any therapeutic effort I know of in the treatment of ringworm. Simpson [98] and Abbe [99] found the keratoses and cancers resulting from roentgen ray burns to be radiosensitive and readily curable with radium. If roentgen rays cause cancer as nitric acid causes destruction, would application of more of the noxious agent be helpful? Roentgen rays cause mutation; mutation leads to tumor formation. The mutation is due to genetic loss. Further application of the agent which produced genetic loss is lethal to cells already genetically deficient.

A small genetic loss should produce comparatively little variation from normal, and some epithelial tumors of the skin, such as trichoepithelioma, closely resemble organized structures. Further loss occasioned by roentgen rays might well disorganize this remaining capacity for organization, with the result of transforming the basal cell tumor into a squamous one, an occurrence which, in fact, is commonplace. With those cutaneous tumors which retain the most organizational power the most roentgen treatment is necessary to kill them, although for the sake of safety the more dangerous squamous cell lesion receives a larger dose from practitioners. A discussion of the degree of genetic loss gives rise to distinctions to which Kyrle [100] has applied the names "homologous" and "heterologous" hamartoma.

If mutations occur naturally, certain mutations would occur fairly commonly, other mutations less commonly and still others in only rare instances. Tumors resulting from mutation should fall into groups, and the groups should possess relative frequencies consistent for a species. This is true in fact and is corroborative of the theory. It may be that there are only a certain number of possibilities altogether, and this can be investigated. The number is probably large.

It is not difficult to believe that in a colony of abnormal cells which are growing only little faster than their normal neighbors an alteration of one component cell leading to great enhancement of its malignant vigor might occur. Mixed tumors and quiescent tumors that suddenly become malignant may be so explained.

K. H. Bauer [101] described unifactoral, multifactoral and chromosomal mutations, so called according to whether the alteration was of one

98. Simpson, F. E.: Illinois M. J. **71**:77, 1937.

99. Abbe, R.: J. A. M. A. **65**:220 (July 17) 1915.

100. Kyrle, J.: Vorlesungen über Histobiologie der menschlichen Haut und ihrer Erkrankungen, Vienna, Julius Springer, 1925, vol. 1, p. 207.

101. Bauer, K. H.: Mutationstheorie der Geschwulst-Entstehung, Berlin, Julius Springer, 1928.

gene, of several genes or even of whole chromosomes; he quoted E. Bauer as having shown that "bud mutations" in plants are due to defects in chromosomal mechanism. Bud mutations consist in the occurrence of a branch with white leaves or a sprout with white flowers on a plant elsewhere bearing colored blossoms. Bauer [101] further stated that there exist in the human being tumor-conditioning, heritable mutations: multiple exostoses, polyposis adenomatosa intestinalis and xeroderma pigmentosum. Dukes,[102] considering intestinal polyposis, said that cancer is not inherited but that the tendency to epithelial proliferation is. The work of Slye [103] constituted the most positive evidence of the inheritance of susceptibility to cancer in mice. She demonstrated incontrovertibly that susceptibility to cancer is inherited as a mendelian recessive in her stock and furnished striking evidence [104] that heredity of a specific type of organ tissue is a fundamental influence in determining the incidence and location of metastatic as well as primary tumors. She [105] showed that Bullock and Curtis,[106] who observed sarcoma of the liver in rats as a result of infestation with Cysticercus fasciolaris, were probably only demonstrating that some animals' tissues regenerate abnormally when irritated. Slye [107] showed that cancer grows rapidly in young and vigorous mice and less rapidly in debilitated, pregnant or aged mice. Voegtlin and Thompson [108] found that diets deficient in lysine resulted in a diminished incidence of spontaneous neoplasia in mice. Voegtlin and associates [109] showed that a deficiency in cystine and methionine caused slowing or cessation of neoplasia. Thus one sees that when normal cells are hard put to it to maintain nutrition, the parasitic cells are likewise. Warthin [110] has reported human families in which the incidence of cancer was astonishingly high. Martynova's [111] studies of the pedigrees of 7,173 persons indicated a real inherited susceptibility to cancer of the breast in the human being.

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102. Dukes, C.: Cancer Rev. **5**:241, 1930.

103. Slye.[7] Slye, Holmes and Wells.[95]

104. Slye, M.: J. Cancer Research **6**:139, 1921.

105. Slye, M.: J. Cancer Research **8**:240, 1924.

106. Bullock, F. D., and Curtis, M. R.: Proc. New York Path. Soc. **20**:149, 1920.

107. Slye, M.: J. Cancer Research **5**:25, 1920.

108. Voegtlin, C., and Thompson, J. W.: Pub. Health Rep. **51**:1429 (Oct. 16) 1936.

109. Voegtlin, C.; Johnson, J. M., and Thompson, J. W.: Pub. Health Rep. **51**:1689 (Dec. 4) 1936.

110. Warthin, A. S.: J. Cancer Research **9**:279, 1925. Further report: Hauser, I. J., and Weller, C. V.: Am. J. Cancer **27**:434, 1936.

111. Martynova, R. P.: Am. J. Cancer **29**:530, 1937.

Reimann and Hall [112] and Hammett and Reimann [113] have been most active proponents of the belief that a cell has three basic properties: proliferation, differentiation and organization. I believe with them that neoplasia is alteration in the organizational property, for differences in proliferative rate occur without neoplasia; differences in differentiation occur without neoplasia, but differences in organization are neoplasia.

Mutation early in embryonic life can lead to teratoma, organoid neoplasia, tissular neoplasia, as in angioma, or localized tumor formation, depending solely on the biologic time of the mutation. As hemangioma is not necessarily present at birth but may make its appearance months or even years afterward, so may mutation bear an antecedent, a coincident or a succeeding relation in time to the event of birth, and the resulting neoplasia may manifest itself at any time. It is, I hope, not metaphysical to consider adolescence, maturity and senescence as features of interest to the embryologist in his capacity as a student of development.

Hammett [114] in 1929 advocated the hypothesis that a stimulus to proliferation of lines of cells with a genetically heightened reactivity to the sulfhydryl group and its mechanism causes cancer. He amply proved in 1930 [115] that the sulfhydryl group does indeed stimulate proliferation. He recognized papilloma formation as due to an increased rate of mitosis. I think that Hammett's explanation should have laid more stress on alteration in organization, rather than proliferation. It is probable that many more mutants come into existence than persist to form visible colonies. I include these, nevertheless, among theoretical neoplastic lesions, but those mutants which through mutation possess a greater than normal rate of proliferation are the actual progenitors of malignant lesions. Reimann and Hall [112] in 1936 showed that the simultaneous action of dibenzanthracene and parathiocresol, expected to enhance carcinogenesis, actually diminished it. I am sure that when malignancy is present the degree of malignancy may be measured by the proliferative rate of the neoplastic as compared with the normal cells; the degree of malignancy is the rate of doing harm.[63] "Malignancy" probably has not the same critical meaning to any two persons who use it.

Muir [45d] has said:

> Cancerous proliferation must not be regarded as all powerful . . . the margin between growth and non-growth is comparatively narrow, and there are numerous

112. Reimann, S. P., and Hall, E. M.: Arch. Path. **22**:55 (July) 1936.

113. Hammett, F. S., and Reimann, S. P.: J. Exper. Med. **50**:445, 1929. Reimann, S. P.: J. A. M. A. **94**:1369 (May 3) 1930; Arch. Path. **15**:675 (May) 1933.

114. Hammett, F. S.: Arch. Path. **8**:575 (Oct.) 1929.

115. Hammett, F. S.: Protoplasma **13**:331, 1931.

examples in the human subject of malignant cells being overcome and disappearing locally. The actual malignancy is in fact the surplus malignancy against tissue resistance.

Many persons have witnessed the disappearance of keratotic lesions from human beings. Mottram [9] remarked the proportion of tar-induced papillomas in mice that disappeared. Smith and later Dunn and Smith [116] reported an astonishing case in which a 23 year old man had multiple squamous cell cutaneous tumors, some of which healed spontaneously.[116a]

Muir [45d] expressed the belief that the following facts are established:

That malignancy may supervene on cellular proliferation brought about in various ways, by irritation, cell stimuli, and hormones, and as a result of compensatory hyperplasia; that in most cases a long period elapses between the onset of proliferation and malignancy; that in cases of chemical substitution the tendency to institute malignancy is in certain instances related to molecular structure; that inherited susceptibility plays an important part, especially in certain organs; that development of malignancy depends in some cases upon congenital abnormality; that these factors may be combined in various ways.

I think the theory of mutation fits these conditions with no undue distortion. Cellular proliferation, however induced, is likely to result, by chance alone, in mutation. If substances chemically associable with vulnerable and significant genes are involved, the mutation is rendered much more likely. The long period that seems to elapse between the onset of proliferation and malignancy is readily explicable either from the standpoint of partial loss of the mutant colony by scaling or by the supposition of malignant following benign mutation. The relation of carcinogenic power to molecular structure is to be expected if carcinogenesis depends on the chemical effect of the agent on the gene. Inherited susceptibility consists of instability of the cell strain. A specific instability related to physical characters is observed in the association of squamous carcinoma of the exposed parts with subnormal pigmentary capacity and excessive actinic sensitiveness on the part of the host. Of one hundred cases of squamous carcinoma of the skin in my records I found ninety instances in which the skin was excessively sensitive to the sun as compared with the skin of the patient's friends and acquaintances. Roffo [117] has provoked the development of carcinoma on depilated areas of white mice by ultraviolet irradiation, the

116. Smith, J. F.: Brit. J. Dermat. **46**:267, 1934. Dunn, J. S., and Smith, J. F.: ibid. **46**:519, 1934.

116a. Concerning spontaneous healing, see Touraine, A., and Duperrat, R.: Bull. Soc. franç. de dermat. et syph. **42**:1727, 1935; Ann. de dermat. et syph. **7**:545, 1936.

117. Roffo, A. H., and Roffo, A. E., Jr.: Prensa méd. argent. **22**:2151 (Nov. 6) 1935; abstracted, J. A. M. A. **106**:166 (Jan. 11) 1936.

earliest lesion being a hyperkeratotic one. Findlay [118] quoted Drabble as having observed one hundred ninety cases of carcinoma of the skin in 955,798 cattle slaughtered in New South Wales. In all but three of them the condition occurred on white areas, and in these three it developed on a branded area. Molesworth [119] has expressed the opinion that cancer of the lower lip exceeds in frequency that of the upper lip because of the exposure of the former to the sun.

A congenital anomaly might occur in material genetically less stable than the remainder of the soma.

The theory of mutation seems to me satisfactory philosophically, biologically and practically. Suggestions as to how it might be proved or disproved would be welcomed by those whose minds seek the truth and grope for inclusive and simple principles that bind many facts together. I do not know how to prove that this theory is true. Nature does the experimenting. The mutations, if that is what they are, take place before one's eyes. Veblen,[120] in a discussion of basic mathematical assumptions, stated:

> The writer is inclined to believe that the truth of a statement can be determined only by testing all its consequences, so that the real test of the validity of the hypotheses of geometry is in the validity of the theorems.

While medicine and mathematics are widely different subjects, the rules of logical thought are uniform in all fields of knowledge. The assumptions requisite to my argument here are: 1. All material life is cellular. 2. All cells come from cells. The implications of the assumption of the theory are consonant with experience.

"Genetic and cytologic evidence," Jones [121] concluded, "is so recent and fragmentary that biologists will hesitate to accept the theory until more critical experimental evidence is available." This is wise and conservative criticism, but the theory has great attraction. It combines multitudes of biologic observations of neoplasia almost as satisfactorily as the evolutionary theory adjusts the normal biologic relationships. Sufficient problems remain, whatever one may believe at a given period of progress.

THERAPY

The problem of treatment may be summed up in the sentence of Dr. Elmer Twyman: "There has never been a carcinoma which could not, *at one time*, have been cured with a hot nail."

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118. Findlay, G. M.: Lancet **1**:1229 (June 7) 1930.

119. Molesworth, E. H.: Dermat. Wchnschr. **99**:945 (July 21) 1934.

120. Veblen, O.: Monographs on Topics of Modern Mathematics, New York, Longmans, Green & Co., 1932, p. 4.

121. Jones, D. F.: Am. Naturalist **70**:86, 1936.

SUMMARY AND CONCLUSIONS

Cancer is a cellular disease. It begins probably in one cell, the progeny of which form a colony of cells, which is the cancer. A solitary cell may possess all the attributes of cancerousness within itself. Histologic evidence shows that carcinoma of the skin in its earliest stages appears to have originated in one cell.

Neoplastic lesions of the epidermis may be classified in accordance with a slow or swift growth of the altered cells and their strong coherence, weak coherence or lack of coherence.

Type I (a).—Strong coherence and slow rate of growth produce senile keratoses, hornlike and verrucous lesions or leukoplakia on mucous membranes, wherein the neoplastic cells closely resemble normal ones and slowly replace them by forming a multilayered disk, the expansion of which results in warping and buckling and produces a warty structure.

Type I (b).—Strong coherence and rapid rate of growth produce carcinoma with a comparatively slight tendency to metastasize and in which the epithelium of "pearls" is multilayered.

Type II (a).—Weak coherence and slow rate of growth produce senile keratoses that scale off readily or erythroplakia on mucous membranes and result in intra-epidermal and subepidermal neoplasia by the spreading of sheets of cells that undergrow the normal ones and substitute themselves for them.

Type II (b).—Weak coherence and fast rate of growth produce rapidly progressive senile keratoses which become carcinomas of intermediate malignancy and in which the epithelial periphery of pearls tends to be of few layers.

Type III (a).—No coherence and slow rate of growth produce intra-epithelial neoplasms of Bowen's and Paget's types and senile keratoses, wherein cells permeate the normal layers and insinuate themselves singly or in small groups among and between normal cells of skin or mucous membrane.

Type III (b).—No coherence and rapid rate of growth produce rapidly expanding intra-epidermal clumps of neoplastic cells, which soon invade the dermis in isolated units, forming carcinomas which metastasize readily.

All neoplasms of the skin in which the cells resemble those of the malpighian layer in undergoing keratinization form a single set, the clinical subdivisions of which are determined by the degree of coherence and the rate of growth.

This theory does away completely with the concept of "precancerosis"; there is no such thing. Small lesions are neoplastic or not

neoplastic; if neoplastic they may grow slowly and be benign or grow fast and be malignant. They should all be destroyed.

The cells of the keratinizing series of cutaneous tumors have a rate of proliferation exceeding normal and differ from normal in appearance, behavior and, probably, genetic constitution. The normal rate of cellular reproduction in the human epidermis approximates one mitosis per day for each basal cell, a total of some 60,000,000,000 mitoses daily. Mutation of one of these cells may initiate and explain the progress and properties of epidermal neoplasia.

The theory of the origin of cancer in somatic mutation is outlined and elaborated. This theory postulates that genetic alteration of a somatic cell may result in the production of a colony which is cancer. The new cells differ from normal ones mainly in rate of proliferation and capacity for organization. Neoplasms transferable by filtrable agents are not satisfactorily explained by the theory.

My observations show how epidermal carcinoma begins from few cells (probably only one cell) and progresses with no fundamental change excepting continued proliferation. My observations are consonant with the theory of mutation.

ABSTRACT OF DISCUSSION

Dr. Everett C. Fox, Dallas, Texas: There is considerable factual evidence of the correctness of the theory of mutation in the origin of cancer. This theory may easily account for the changes seen in cutaneous carcinoma, with the frequent divisions of cells which may be influenced by many external factors, such as exposure to sunlight, trauma, chronic inflammation and irritation. It is really surprising that abnormal division is not evidenced more frequently.

I cannot agree with Dr. Sutton in his hypothesis that carcinoma is always a neoplasm from the earliest clinical lesion. There are too great a number of conditions, both clinically and histologically, which may eventuate in cancer. Carcinoma at times develops in many relatively simple inflammatory processes. It may be superimposed on perfectly typical lupus erythematosus or lupus vulgaris. It has been seen to develop in a sebaceous cyst, the neoplasm beginning in a small area, and has been known to develop frequently at the site of previous cystic disease of the breast. The conditions present definite histologic pictures first of an inflammatory and later of a neoplastic process. The frequency of syphilis of the tongue with subsequent carcinoma can hardly be questioned. Leukoplakia is an inflammatory process and even when verrucous has not necessarily become malignant. When carcinoma develops there have been the preceding characteristic inflammatory changes.

I am unwilling to concede that the first irritation of the buccal mucosa from an irregular tooth or denture, though it becomes malignant, was neoplastic from the early inflammatory stage. This statement may be applied to the early inflammation in tar-induced carcinoma and other repeated irritative and inflammatory processes. A burn of several years' duration in which keratosis and later carcinoma develop was not neoplastic from the beginning.

Many inflammatory processes show acanthosis, hyperkeratosis, parakeratosis and even dyskeratosis, with inflammatory changes of cells and nuclei, by altered staining reactions but do not have the definite characteristics of neoplasm. To prove his statements Dr. Sutton must be able to diagnose cancer from one cell and differentiate it from adjacent normal cells and cells altered by inflammation. Diagnosis of this type is being advanced by the use of "needle biopsies," especially of lesions of the breast, but is still inaccurate and inconclusive.

Carcinoma probably begins in a single cell from an abnormal cell division. This occurs more frequently in cells that divide more rapidly than normal and therefore are seen to develop more frequently in areas of inflammation, in which there are more mitoses. Hence, cutaneous malignancy is more likely to begin in an abnormal area of skin than in a normal one. This is frequently observed by dermatologists.

I should prefer to believe that carcinoma begins in a cell changed by previous inflammation and that atypical cell division, or mutation, occurs as a result of this process. If there are 60,000,000,000 mitoses daily in normal skin, there are several times this number in an inflamed epidermis. Consequently, according to the theory of mutation, cancer is more likely to develop, and on this basis any epidermal inflammation is potentially precancerosis.

Dr. Fred Weidman, Philadelphia: The presentation is closely reasoned and philosophical. It may be resolved into two parts, the first being a discussion of the mechanism whereby a particular morphologic picture is induced, as seen histologically, i. e., a matter of the coherence of cells. It appears to me that the same mechanism should apply not only to senile keratosis, verruca vulgaris, etc., but to lesions which are not precancerous, as, for example, psoriasis, lichen planus and blastomycosis. I simply cite those few; the list could be enlarged. Under the differing conditions of coherence and noncoherence of cells, I feel sure that one could accumulate a series of such dermatoses parallel to those which Dr. Sutton has cited as bearing on cancer.

After that, it seems to me that the only circumstance which remains in the differentiation between the precancerous and the nonprecancerous states is the matter of growth, and that must bring the discussion down to the one problem which is occupying the minds of all dermatologists as to the cause of cancer. As I understand it, mutation is brought into the situation, and I should like to know rather more definitely from Dr. Sutton what he means by mutation—whether his use of the term is parallel to that of most biologists, i. e., a more or less permanent change in preexisting qualities. Perhaps Dr. Sutton refers to such a phenomenon as anaplasia. I take it that by mutation he refers to changes in the chromosomes —changes of such an order as will eventuate in abnormalities of growth.

Dr. Richard L. Sutton Jr., Kansas City, Mo.: I think it is impossible to accept the theory of mutation in the origin of epidermal tumors and at the same time to accept the concept of precancerosis. They are, logically, mutually incompatible. Lupus erythematosus is not precancerosis, because it is lupus erythematosus until there develops on a small part of it a new lesion which is not lupus erythematosus but small and early carcinoma, which spreads from that centrum. The word "lesion" is confusing. It is easy to use it to mean a number of different spots, whereas I wish to use "lesion" as a particular spot on a particular person at a particular time.

Dr. Fox's statements regarding leukoplakia I flatly deny. That condition is not inflammatory. How many of the members have seen the fulguration of a

leukoplakic area introduce the cells into a subepidermal region so that a vegetative carcinoma results? The way to get rid of leukoplakia is simply to take a little red hot iron, a small soldering iron or a Post cautery, and blister it off. All the cells are killed at once then.

The irritation which leads to carcinoma, according to the theory of mutation, does so by causing cellular mitosis, and the mitosis goes wrong. Those areas of a blond and sun-sensitive person which are exposed to sunshine undergo mitosis; the surface cells of those areas mitose a great deal more frequently than normal ones, in all probability, although this has not been thoroughly investigated. However, such areas certainly do sunburn easily, and on the fair-haired farmer of Kansas whose skin is irritated and perhaps genetically altered by the sunshine, colonies of mutants develop, each appearing as a keratosis which looks like the result of dropping a bacterium into a Petri dish. It grows expansively. No one can say whether the primary irritational lesion is early cancer or an inflammatory lesion; a cancer may begin at any point.

Grouping is dependent on the behavior of the cells, and it is impossible to watch under the microscope the behavior of one cell that has been pickled in formaldehyde. Malignancy is a clinical and dynamic term applicable to living tissue, and it is not the prerogative of a pathologist to put it into dead tissue. When he calls dead tissue malignant he is saying, "I have seen dead tissue from other lesions which looked like this and which turned out to be malignant."

"Malignant" is a slipshod term, used glibly without criticism. "Malignancy" implies a genetic alteration of type, plus capacity to do harm, and the degree of malignancy is the rate of doing harm. Any proliferating cell in a metazoan animal is a potential carcinoma, because it can undergo genetic alteration, and so a metazoon as a whole is a precancerosis. Every living creature is the result of the proliferation of one fertilized ovum. Some strains may be more susceptible to genetic alteration than other strains, as the geneticists have shown.

Dr. Weidman's interpretation is, to my notion, a most excellent one, and I do not see how he conceived it in fifteen minutes. I agree with him that what I showed is only that the morphologic picture, grossly and microscopically, is dependent on the adhesiveness of the cells to each other and is explicable by physical phenomena. The physiologic characteristics of the lesion are functions of the rate of growth, and similar considerations are wholly applicable to anything that is composed of cells. The cells shown, however, are genetically altered cells; their ancestral cell has been damaged as by roentgen irradiation, which has been known to cause the loss of chromosomes. Application by Patterson and Miller of roentgen radiation to germinal cells produced inheritable alteration in the soma; its application to multicellular larvae resulted in development of patches of abnormal tissue instead of a complete somatic alteration, only the progeny of the altered cell being different from the remainder of the soma. Such somatic mutations are not inheritable.

There is a wholly adequate biologic background for these assertions.

The rate of growth is the criterion of malignancy. The metastasis breeds true. The cells of the metastasis are exactly like those of the primary lesion. Yes, the alteration is permanent. The metastatic cells in the lung and the liver are just like those in the primary lesion and those in the lymph gland, and the alteration need be applied to only one cell, which is an ancestral cell, and all its progeny are the same from then on.

There is no numerical change in chromosomes. This has been tested. Boveri's conception was that peculiar mitoses led to variations in the number of chromosomes, but chromosome counts have not shown this. A genetic alteration need not

involve an entire chromosome. The theory of mutation is the theory of R. C. Whitman, professor of zoology at the University of Colorado. His paper of 1919 was the one that led me into this line of thought. I offer evidence which, I think, supports that theory.

Mr. James Brooks, of the Photographic and View Company, of Kansas City, finished the photos. The sections have been chosen from a series of over 1,000 lesions removed in private practice. They were cut and stained in the laboratory of the Royal College of Physicians, of Edinburgh, Scotland, under the direction of Col. W. F. Harvey, who possesses a duplicate series which is available for examination.

HENRY GRANGER PIFFARD

A GREAT FACTOR IN THE PROGRESS OF AMERICAN DERMATOLOGY

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NEW YORK

In the last half of the nineteenth century there existed in America a small group of distinguished men whose devotion to dermatology knew no bounds. Endowed with the excellent training and inspired by the example of the French, English and Austro-German schools of that period, they became through their own efforts leaders in the field of this ever fascinating specialty and founded in this country so splendid a dermatologic structure that, while one may admire the gold leaf applied rather thickly on its cupola by its most recent disciples, it is the main structure which commands one's love and reverence. Prominent in this small group was Henry G. Piffard, genial fighter, avid hobbyist, profound thinker, forceful teacher and splendid dermatologist. Piffard was born in the town of Piffard, N. Y., on Sept. 10, 1842. He graduated from the University of the City of New York in 1862 and received his medical degree from the College of Physicians and Surgeons in 1864. He became greatly interested in dermatology soon after graduation and left for Europe to perfect his training in the specialty. He spent considerable time in Paris and Vienna, but most of his postgraduate work was done under the tutelage of Dr. Tilbury Fox at the University College Hospital in London. It was in the dermatologic clinic of that hospital that he first met a fellow countryman from New York, Dr. George Henry Fox, who was also doing postgraduate work in dermatology. The two men immediately became close friends and remained so until the death of Piffard nearly forty years later. The friendly association of these two men for nearly half a century can be understood readily by those fortunate enough to have been acquainted with both of them, thereby realizing how much they accomplished in establishing a firm foundation for the specialty they both loved, not only in New York but in the world at large. It was from George Henry Fox that most of the knowledge of Piffard's personal side was obtained. His reminiscences of Piffard[1] are fascinating reading for every dermatologist.

1. Fox, G. H.: J. Cutan. Dis. **29**:82, 1911.

Piffard on his return from Europe established himself in New York and within a year or two published an excellent translation of Hardy's "The Dartrous Diathesis, or Eczema and Allied Affections." This book appeared in 1868, and by then Piffard had already become an attending dermatologist in the dermatologic clinic at the Bellevue Hospital. A year later, in 1869, in association with Faneuil D. Weisse, Henry Daggett Bulkley and Foster Swift, he signed a famous letter,

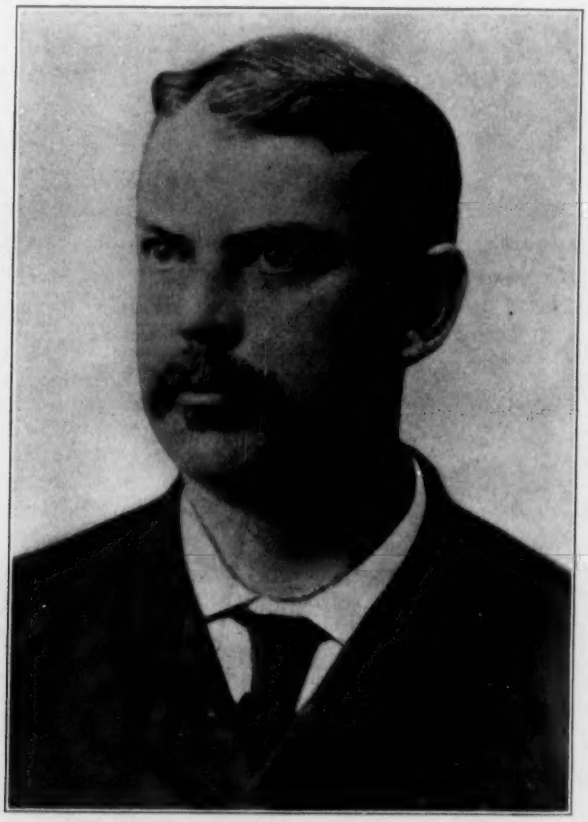

Fig. 1.—Dr. Henry Granger Piffard as a young man (collection of Dr. Howard Fox).

which was sent to various New York dermatologists. It read as follows:

Knowing as we do that you are interested in dermatology, we would wish you to participate with us in the organization of a society to be devoted to the investigation and consideration of the same. The object of the "New York Dermatological Society" shall be to afford all those interested in this most important department of medicine an opportunity for a full exchange of their opinions and methods of

practice, and to contribute American experience and investigations to the fast accumulating stock of our knowledge of diseases of the skin.

In response to this letter the oldest dermatologic society in the world was organized on May 18, 1869, at the house of Dr. Henry Daggett Bulkley, 42 East Twenty-Second Street.

In 1871 Piffard was appointed visiting dermatologist to the City Hospital, the first institution in the United States to establish dermatologic wards. He served in this capacity until 1885, when he was appointed consulting dermatologist. During this service at the City Hospital, Piffard, instead of arriving in a stream-lined automobile, was wafted gently to the surface of the island by an elevator and crossed the river in a rowboat manned by convicts; occasionally in storms and when the tide was unusually strong it took several hours to get across. The weather was so severe at times that he remained marooned on the island for several days. The male nurses and orderlies of the hospital were all convicts at that period, and getting drunk was their favorite recreation; as Piffard stated, whisky was the coin of the realm on the island. He on one occasion reached the river front on a particularly stormy day and could get only a solitary boatman to ferry him over. The trip was so arduous that it was impossible to return; so Piffard ordered a bed for his boatman. A week later the boatman visited him suffering from severe scabies, the drunken orderly having put him in the same bed with two patients suffering from scabies.

Piffard became professor of diseases of the skin in the medical department of New York University in 1874 and served this institution for many years. He was its emeritus professor at the time of his death. His lectures, while not gifted with soaring rhetoric, were practical, interesting and forceful.

In 1876 he published his well known "Elementary Treatise on Diseases of the Skin." It was the second textbook on cutaneous diseases to be published in America. In that same year he helped to found the American Dermatological Association. In 1881 his "A Treatise on the Materia Medica and Therapeutics of the Skin" appeared. He contributed many excellent articles to various medical journals throughout his career. I have in my possession the first volume of the first journal devoted to dermatology in America, *The American Journal of Syphilography and Dermatology.* It appeared in 1870 and is a presentation copy to Professor Samuel D. Gross, signed by the editor, M. H. Henry. On page 217 is an article by Piffard describing his method of taking and preparing biopsy specimens for microscopic study. According to Andrew R. Robinson, Piffard deserved the credit for the use of the term tuberculid, as he defined it in 1892, four years before Darier's work on the subject.

Piffard's superabundant energy, coupled with the brilliant, many-faceted mind of a near-genius, brought him international recognition. Another striking characteristic was his extraordinary will-power. He would devote his entire time to whatever subject he was interested in at the time, working night and day to accomplish his end. At times, before he was half through, he would drop everything and choose another subject of equal interest, which he would pursue with equal vehemence. This erratic method unfortunately did much to prevent what might well have developed into great medical discovery.

Piffard was never without a hobby. To these multitudinous hobbies he would devote all the energy of his mind and body and would at times astound experts with the profundity of his knowledge on the subject. He was at one time interested in ballistics and invented an apparatus for lessening the recoil of a gun which was commented on favorably by officers of the United States Army. At other times he would discuss botany, electricity, microscopy, photography or ichthyology in such a learned manner that his listeners would decide that he had devoted a lifetime to that particular subject. It was easy to determine what hobby he was riding at the time by the appearance of his office. Dr. George Henry Fox described its appearance as follows:

> When I first visited him I generally stumbled over a number of galvanocauteries and had hard work to find a chair unoccupied by zinc and carbon plates, or unspotted with bichromate solution. Later, I have seen a fishing rod in each corner, and reels upon almost every shelf of his library. Again I have noted at least a half a dozen rifles of various makes and failed to count the cartridges scattered upon his office desk. In recent years, the guns and rods had gradually disappeared. The microscopes and the mounted photographs still clung to his desk like old friends, but the general aspect of his office had changed and was more suggestive of an electrical show at the Madison Square Garden.

Piffard's hobbies were the cause of many amusing incidents. At one time he conceived the idea of becoming adept with the banjo. After one lesson he retired to his home with a brand new, expensive instrument and after a week's practice returned to his teacher, who after listening patiently to Piffard's efforts took the banjo from him and strummed a tune on it. After a negative reply from Piffard as to his knowledge of the tune he was playing, the teacher told him it was "Carry Me Back to Ole Virginny," the same tune Piffard had been practicing at home for a week. At another time he ordered from his book dealer an expensive Italian monograph, presumably on some dermatologic subject. The book dealer told him in trepidation that the book was worth $60, whereupon Piffard in anger told him that he did not give a damn about the price; all he wanted was the book. In due time it arrived, and to Piffard's dismay it turned out to be an elaborate treatise on the tanning of hides.

Dr. George Henry Fox, to whom these anecdotes on Piffard must be attributed, stated that when he met him at Tilbury Fox's clinic at the University College Hospital in London he was tall, straight and handsome and wore black curling side-whiskers. Later in life the side-whiskers were joined by a Vandyke beard, which later became gray, but he always remained handsome, and his entire appearance, especially his keen eyes, mirrored his open and genial character.

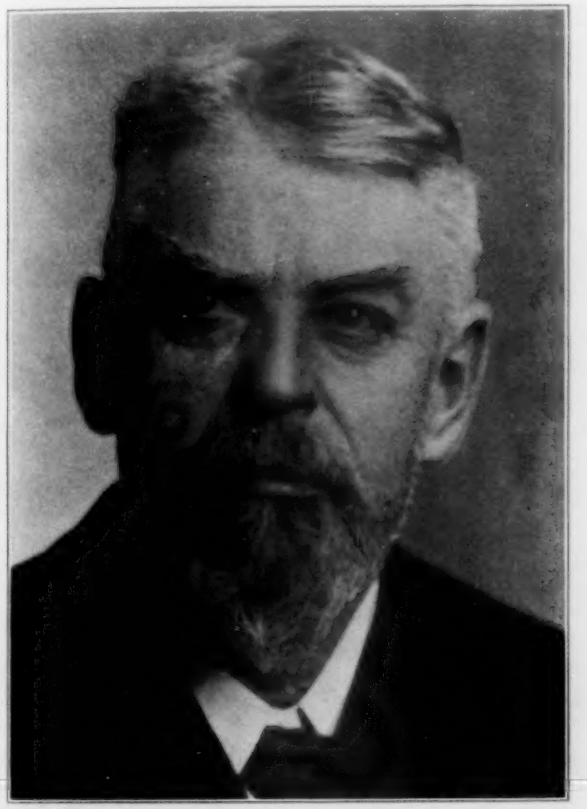

Fig. 2.—Dr. Piffard at the height of his career (collection of Dr. Howard Fox).

Piffard, despite advancing age, never allowed his energy to diminish. He continued to work at high pressure, either on some particular branch of dermatology or on one of his beloved hobbies. It may be that through his love of work he lowered his resistance to disease, for he died of pneumonia on June 8, 1910, at the age of 68, after only three days of illness. In his passing his intimates lost a genial, fascinating, kindly man; the New York Dermatological Society, a good debater whose

remarks were valuable, instructive and always to the point, and the dermatologic world at large, a tireless, brilliant worker whose efforts were always directed where they could accomplish the most good for dermatology as a whole, rather than for himself. Henry Granger Piffard will never be forgotten. As George Henry Fox aptly put it, he was "a blazing meteor in our dermatologic firmament," and a blazing meteor he will remain to students and lovers of dermatologic history.

APLASTIC ANEMIA FOLLOWING USE OF NEOARSPHENAMINE

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The toxic effects following the use of arsenical preparations in the treatment of syphilis have been known and reported in the literature since the introduction of arsphenamine by Ehrlich in 1910 and of neoarsphenamine in 1912. Hemorrhagic phenomena were first noted by Rumpel [1] in 1910 and by Leede [2] in 1911. Labbé and Langlois [3] first drew attention to the importance of blood dyscrasia in 1919. Other reports of the toxic effects of arsenicals have been made by the Medical Research Council of Great Britain [4] in 1922, by Kerl [5] in Jadassohn's *Handbuch* in 1928, by Phelps and Washburn [6] in 1930 and by Cole and his associates [7] in 1931.

Farley [8] in 1930 collected thirty-nine cases of damage to the bone marrow following the use of arsenicals in antisyphilitic therapy and

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From the services of Drs. Leon Unger and Frederick Tice, Cook County Hospital.

From the department of pathology, Dr. R. H. Jaffé, director, Cook County Hospital. Dr. Jaffé, who died on Dec. 7, 1937, performed both autopsies and made the microscopic diagnosis.

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2. Leede, C.: Zur Frage der Behandlung der Anämie mit Salvarsan, München. med. Wchnschr. **58**:1184, 1911.

3. Labbé, M., and Langlois, S.: Purpura hémorragique aigu par intoxication arsénicale, Bull. et mém. Soc. méd. d. hôp. de Paris **43**:786 (July 25) 1919.

4. Reports of the Salvarsan Committee: II. Toxic Effects Following the Employment of Arsenobenzol Preparations, Medical Research Council, Special Report Series, no. 66, London, His Majesty's Stationery Office, 1922, pp. 4-94.

5. Kerl, W.: Salvarsanschädigungen, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, vol. 18, p. 604.

6. Phelps, J. R., and Washburn, W. A.: Toxic Effects of Arsenical Compounds Employed in Treatment of Syphilis in the United States Navy, Urol. & Cutan. Rev. **34**:458 (July) 1930.

7. Cole, H. N.; DeWolf, Henry; McCuskey, J. M.; Miskjian, H. G.; Williamson, G. S.; Rauschkolb, J. R.; Ruch, R. O., and Clark, Taliaferro: Toxic Effects Following Use of the Arsphenamines, J. A. M. A. **97**:897 (Sept. 26) 1931.

8. Farley, D. L.: Depressed Bone-Marrow Function from Arsphenamins, Including Type of So-Called Agranulocytosis, Am. J. M. Sc. **179**:214 (Feb.) 1930.

added seven others, in only two of which there were findings of aplasia of all elements of the bone marrow. Stephens [9] in 1931 added two cases, in one of which complete aplasia of the bone marrow was found while in the other there were islands of active regeneration.

McCarthy and Wilson [10] collected seventy-nine cases of all types of blood dyscrasia after a careful search of the literature. Only thirty-four cases were classified as instances of aplastic anemia, and in only six of these did the patient recover, making a mortality of 83 per cent. In these cases it was noted that the onset of aplastic anemia occurred after a short course of injections, often but one or two doses of the drug having been used.

Reports of blood dyscrasia following the use of arsenicals have become more numerous in the recent literature, especially those of purpura haemorrhagica, which is the most common type. Agranulocytosis, which is less common, has been observed on several occasions. Aplastic anemia is the least common and the most fatal of the complications in the bone marrow, and but seventeen cases have been reported since McCarthy and Wilson's [10] summary of cases (Bronfin and Singerman,[11] Loveman,[12] Semenza,[13] Fieschi and Baccaredda,[14] Sézary and Lenègre,[15] Bennett and Pritchard,[16] Bruni,[17] Bertrand and Simard,[18] Stephens,[19]

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9. Stephens, D. J.: Aplastic Anemia Occurring During the Treatment of Syphilis with the Arsphenamines, Am. J. Syph. **15**:333 (July) 1931.

10. McCarthy, F. P., and Wilson, R., Jr.: The Blood Dyscrasias Following the Arsphenamines, J. A. M. A. **99**:1557 (Nov. 5) 1932.

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12. Loveman, A. B.: Toxic Granulocytopenia, Purpura Hemorrhagica and Aplastic Anemia Following Arsphenamines, Ann. Int. Med. **5**:1238 (April) 1932.

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17. Bruni, G.: Le mielotossicosi da novarsenobenzolo (con contributo casistico), Clin. med. ital. **65**:583 (June) 1934.

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Merkelbach,[20] Knott,[21] Imrie,[22] Levi and Robba,[23] Smith and Lyon,[24] Pepino,[25] Girard and Vérain [26] and Prévot, Simonin and Vérain.[27]

To these fifty-one cases I wish to add three, which were observed at the Cook County Hospital from 1929 to 1936. (Many cases of blood dyscrasia following ingestion of arsphenamine preparations have been observed, but these three are the only ones classified as instances of aplastic anemia.)

REPORT OF CASES

CASE 1.—A white woman aged 25, a telephone operator, was admitted with the provisional diagnosis of purpura haemorrhagica. She complained of weakness and anemia for the past year and had been treated with liver extract. Three months prior to admission she noted increased weakness, bleeding from the gums, tarry stools, menorrhagia and spotty vaginal bleeding (metrorrhagia). One week before admission she had to stop working and go to bed. At the time of admission bleeding from the gums was marked, and a profuse bloody vaginal discharge was present. Examination of the blood revealed severe anemia (560,000 erythrocytes) and leukopenia (2,600 leukocytes).

A transfusion of 500 cc. of citrated whole blood was given immediately, and bleeding stopped, only to recur later. The erythrocyte count was elevated by the transfusion, but the white blood cells progressively decreased. On additional questioning the patient disclosed that she had had a secondary generalized syphilitic eruption two and one-half years previously and had received intensive antisyphilitic treatment, totaling forty intravenous and five intramuscular injections of neoarsphenamine and a bismuth preparation (dosage unknown). Treatment had continued despite the presence of marked anemia and progressive weakness. A yellow tint of the skin appeared. The last injection of neoarsphenamine was give two weeks prior to admission.

Physical examination showed no abnormality except for spongy bleeding gums, a bloody vaginal discharge, a yellow tint to the skin, tarry stools and flame-shaped retinal hemorrhages. A septic temperature curve was noted.

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26. Girard, N., and Vérain, M.: Aleucie hémorragique mortelle consécutive à un traitement mixte arséno-bismuthique, Rev. méd. de l'est **63**:809 (Dec. 1) 1935.

27. Prévot; Simonin, and Vérain, M.: Aleucie hémorragique mortelle au cours d'un traitement arséno-bismuthique, Rev. méd. de Nancy **64**:60 (Jan. 15) 1936.

Clinical Course.—The patient received a total of four blood transfusions of 500 cc., but she grew progressively worse and died on Nov. 23, 1936. The leukocyte count on the day before death showed but 450 cells. Additional therapy included administration of cevitamic acid (vitamin C), 50 mg. daily, whole bone marrow, liver extract orally and subcutaneously (1 ampule being equivalent to 4,800 Gm. of whole liver), sodium thiosulfate intravenously, blood intramuscularly, calcium gluconate, vitamins A, B and D, hydrochloric acid and inorganic iron. Laboratory examination of the gastric contents after ingestion of the Ewald meal showed 2 degrees free hydrochloric acid, 5 degrees combined hydrochloric acid and 7 degrees total acid. No blood was found. The bleeding time was more than one hour, and the coagulation time was four and one-half minutes. Chemical examination of the blood revealed 15 mg. of urea nitrogen per hundred cubic centimeters. Smears of material obtained by sternal puncture revealed almost complete absence of myeloid elements. A few lymphocytes and normoblasts only were seen. The basal metabolic rate was + 3 per cent. The Kahn reaction was questionable on two occasions and 1 plus on the third examination.

The essential findings at autopsy were as follows: Purple-gray and red-brown patches ranging in size from that of a pinhead to 3 by 5 mm. were found in the skin, under the epicardium and the endocardium and in the renal pelvis. On the inside of the upper gum there was an irregular defect in the mucosa of about 10 by 15 mm., which was covered with foul-smelling dirty brown material. Microscopic examination of the marrow of the femur showed that the cellularity varied between 45 and 85 per cent. The differential count showed 12.4 per cent myeloblasts, 4 per cent neutrophilic myelocytes, 1 per cent eosinophilic myelocytes 0.8 per cent eosinophilic leukocytes, 6.4 per cent erythroblasts, 18 per cent normoblasts, 43 per cent lymphocytes, 8.2 per cent plasma cells, 0.8 per cent young megakaryocytes and 5.4 per cent erythrophages. Of the cells included in the group of myeloblasts, some were typical myeloblasts with basophilic cytoplasm and round, pale nuclei containing prominent nucleoli. Others were large, their nuclei indented and their nucleoli elongated. These cells resembled megakaryoblasts. There were smaller forms, with nuclei of more compact chromatin structure, approaching the hemocytoblastic stage. These different cell forms were linked together by transitional forms so that an exact numerical determination of each form was impossible. The neutrophilic myelocytes were poorly preserved, the granules, especially, appearing as ill defined light pink droplets. Among the plasma cells there were large binucleated forms. There was a moderate amount of blood pigment in the swollen reticulum cells.

On chemical analysis 3.165 Gm. of hair and nails yielded 0.009 mg. of arsenic, calculated as arsenic trioxide; 275 Gm. of liver yielded 2.53 mg. of arsenic, calculated as arsenic trioxide, equivalent to 0.92 mg. per hundred grams; 170 Gm. of kidney yielded 0.95 mg. of arsenic, calculated as arsenic trioxide, equivalent to 0.56 mg. per hundred grams.

The anatomic diagnosis was: severe generalized anemia of the hypoplastic type; slight hypertrophy of the heart, anemia and fatty degeneration of the myocardium; fatty changes and hemosiderosis of the liver; acute emphysema of the lungs; hemorrhage into the uterine cavity; hemorrhagic corpora lutea; gangrenous stomatitis, and petechial hemorrhages in the skin, underneath the epicardium, the endocardium and the renal pelvis and in the mucosa of the colon.

Case 2.—A Negro woman aged 30 complained on admission of bleeding gums and spotty vaginal bleeding for one week. In 1929 she had had acute pelvic peritonitis. In 1930 treatment for syphilis was started. This treatment was given

intensively after October 1934. She had received her last injection the day before admission, one week after first noting ptyalism, metrorrhagia, fever, bleeding gums and mild sore throat, which became worse the day of admission.

Physical examination showed no abnormality except markedly carious teeth and bleeding gum margins with a brown-black line between gums and teeth; a systolic murmur was heard at the base and at the apex of the heart, and the corpus uteri was enlarged and irregular and had a bloody discharge. The temperature was 101.6 F., and the blood pressure, 125 systolic and 80 diastolic. Laboratory examination of the blood on admission revealed 900,000 erythrocytes, 1,900 white blood cells and a hemoglobin content of 30 per cent, determined by the Tallqvist method. The coagulation time was three minutes and the bleeding time twenty minutes. Smears of the blood showed only small lymphocytes. The sedimentation time was five minutes (complete). The Kahn reaction was 2 plus. Chemical analysis of the blood revealed 49.5 mg. of urea nitrogen and 3.15 mg. of creatinine per hundred cubic centimeters. A transfusion of 700 cc. of citrated whole blood was given, and 3.5 cc. of liver extract (equivalent to 2,800 Gm. of whole liver) was administered subcutaneously. The course was progressively downhill. The patient became delirious and psychotic; a septic temperature curve was noted, and the ulcerated lesion of the mouth spread to include the tonsillar fauces. She died on June 25. At no time was any evidence of regeneration of the blood noted. Autopsy showed dark purple-red areas of consolidation in the lower lobes of the lungs. The myocardium was light brown-gray, mottled with darker purple-red. Underneath the endocardium purple-red patches up to 5 by 5 mm. were noted. Similar hemorrhages were present in the mucosa of the stomach and the renal pelvis. The fimbriated ends of the fallopian tubes were occluded and fused with the ovaries. In the left ovary a cyst 7.5 by 7 by 5 cm. extended into the broad ligament, which was filled by dark red, coagulated blood.

Microscopic examination showed the marrow of the femur to be fatty and the capillaries between the fat cells moderately congested. Near the capillaries was an occasional small nest of cells, not larger than a high power field. These nests consisted chiefly of plasma cells, some of which were fairly well preserved, although the majority showed alterative changes in the form of pyknosis of the nucleus and vacuolation of the cytoplasm. Myeloid cells were exceedingly scanty. It took considerable search to discover a few neutrophilic myelocytes or metamyelocytes and a few normoblasts. The normoblasts were of medium size with scanty cytoplasm; the myelocytes were relatively small; the granules stained poorly, and between the granules there were occasional fine vacuoles. There were also a few oxyphilic leukocytes, which were much better preserved. Megakaryocytes were absent. The reticular cells were swollen and contained single erythrocytes and dark brown and pale green-brown granules of pigment. In addition to the small cell foci which were wedged between the fat cells, the marrow contained an occasional nodule made up of small and medium-sized lymphocytes and a few free histiocytes. Some of these nodules showed a loose net of fibrin between the lymphocytes. The microscopic examination of other organs did not disclose anything unusual.

The anatomic diagnosis was: severe generalized anemia of the aplastic type following administration of arsphenamine; petechial hemorrhages in the epicardium, the endocardium, the myocardium, the diaphragm and the renal pelvis; pseudomembranous colpitis; confluent bronchopneumonia in the upper lobe of the right lung and the lower lobes of both lungs, and fibrous adhesions about the uterus, the tubes and the ovaries and recent hemorrhage into a tubo-ovarian cyst of the left side.

On chemical analysis 1.285 Gm. of hair and nails gave no indication of arsenic; 570 Gm. of liver yielded 13.6 mg. (0.21 grain) of arsenic trioxide; 120 Gm. of kidney yielded 2.88 mg. (0.04 grain) of arsenic trioxide.

CASE 3.—A markedly emaciated white woman 23 years of age was admitted to the hospital with the provisional diagnosis of agranulocytic angina, based on a history of sore throat for two and one-half weeks and weakness, anemia, pallor, cough and bloody sputum for one week. She had had a cutaneous disease diagnosed as "psoriasis" for "years" and in the past eight weeks had had four injections of neoarsphenamine (dosage unknown). Three months before admission she had had bleeding gums. Eight weeks before, she had had sore throat following injections of the drug. For one week prior to admission she had had to remain in bed because of extreme weakness and fever.

The physical examination revealed an acutely ill white woman with a temperature of 102.8 F., a pulse rate of 112 and blood pressure of 115 systolic and 65 diastolic. The lining of the throat and the gums were thickened and soft and oozed blood. They appeared foul and ulcerated and were covered with a thick gray membrane. There were petechiae in the conjunctivae. The cervical lymph nodes were large, tender and discrete. There was a systolic murmur at the apex. The spleen was not palpable. Large ecchymoses and a few petechiae were noted on the extremities, the skin being markedly indurated. Laboratory examination of the blood revealed severe anemia, neutropenia and a low platelet count. The bleeding and the coagulation time were normal. Smears of blood revealed anisocytosis, poikilocytosis and slight macrocytosis. The Kahn test was negative. The patient was given pentnucleotide, concentrated liver extract subcutaneously and blood intramuscularly. A donor for blood transfusion was not available. She became delirious and died on June 13. The hair and the nails were examined for arsenic but showed none. Permission for autopsy was refused.

COMMENT

Classification.—McCarthy and Wilson [10] classified blood dyscrasias following injection of arsphenamine in three main groups: (1) thrombopenic; (2) granulocytopenic and agranulocytic, and (3) aplastic. In addition, a few cases with entirely atypical manifestations were discussed separately. On this basis the prognosis was determined. In the first group the essential feature is acute thrombopenia, with no evidence of depression of the bone marrow. The second group includes forms in which there is depression only of the granulocytic elements, with little change in the number of erythrocytes and platelets. Aplastic anemias comprise the third group, in which all the cellular elements of the bone marrow are affected. The prognosis in cases of group 1 is good. In group 2 there is a much less favorable prognosis, with a mortality rate of approximately 33 per cent. In group 3 the prognosis is grave, and the mortality is high. Purpura haemorrhagica associated with severe anemia has been noted on many occasions, but in cases of that combination there is evidence of regeneration of the bone marrow, so that such cases must be ruled out in the differential diagnosis. Pseudo-aplastic

anemia,[28] in which the bone marrow is normal or even hyperplastic, is ruled out by sternal puncture.

Predisposing Factors.—It has been noted that the condition occurs most frequently in young white women. The arsenical preparations which have produced blood dyscrasia include: arsphenamine, neoarsphenamine, stovarsol,[24] sulfarsphenamine [19] and silver arsphenamine. Tryparsamide had been used in but one reported case, but in combination with other preparations of arsphenamine, so that it cannot be contemplated as an etiologic factor. The doses used and the number of injections of the arsenical preparation varied greatly, and while intervals of from one hour to four months have previously been noted, in the majority of cases the condition becomes evident after a few injections and a short course. The interval, however, may be prolonged. In one of the three cases reported there was a history of weakness and anemia for a year, with bleeding from the gums for three months. Fatalities have been noted after two or three injections of the usual dosage. Cole and his associates [7] pointed out that the type of drug used is a great factor. Stokes [29] expressed the belief that aplastic anemia causes 5 per cent of the deaths following arsenical treatment and stated that it must be watched for, especially in patients who do not do well under treatment.

Cases of allergy to arsphenamine and neoarsphenamine were discussed by Stokes. Asthma and urticaria following contact with neoarsphenamine have been reported by Sulzberger,[30] and another case involving that association [31] has been mentioned to me. Stokes discussed the possibility of production of sensitivity by leakage into the subcutaneous tissue during intravenous injection. Vitamin C may be a factor in sensitization, and Daïnow [32] reported four cases in which there had been reactions to treatment with arsphenamine and in which there was response to intravenous injections of cevitamic acid (vitamin C). Causative roles have also been attributed to other vitamins, and maintenance of a diet sufficient in vitamins has been advised.

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28. Jaffé, R. H.: The Bone Marrow, J. A. M. A. **107**:124 (July 11) 1936. Thompson, W. P.; Richter, M. N., and Edsall, K. S.: An Analysis of So-Called Aplastic Anemia, Am. J. M. Sc. **187**:77 (Jan.) 1934.

29. Stokes, J. H.: Modern Clinical Syphilology, ed. 2, Philadelphia, W. B. Saunders Company, 1934.

30. Sulzberger, Marion B.: Studies in Tobacco Hypersensitivity, J. Immunol. **24**:85 (Jan.) 1933.

31. Unger, L.: Personal communication to the author.

32. Daïnow, I.: Note préliminaire sur l'action désensibilisante de l'acide l'ascorbique (vitamine c): Guérison rapide d'un cas d'intolérance au salvarsan, de trois cas d'érythrodermie salvarsanique et d'un cas d'érythrodermie aurique, Ann. de dermat. et syph. **6**:830 (Sept.) 1935.

Mechanism.—The mechanism by which the arsenical preparations produce these reactions has caused much speculation. McCarthy and Wilson [10] suggested that the benzene radical may be the responsible factor, since it is common to all the arsenicals used and has been known to produce aplastic anemia. Inorganic arsenic compounds have not been known to produce damage to the bone marrow, and in but one case has granulocytopenia been reported following the use of inorganic arsenic.[33] However, the benzene radical cannot be held to be the cause of acute thrombopenia, although the platelets have been found to diminish during the course of treatment.[34] Smith [35] expressed the belief that the condition is due to "platelet crisis," i. e., rapid destruction of the platelets in the blood stream without effect on the megakaryocytes. McCarthy and Wilson concluded that this reaction is "anaphylactoid." In view of the finding of relatively large amounts of arsenic stored in the liver and the kidneys in the two cases reported here, it may be suggested that the changes may be due to the effect of the arsenicals on the liver itself. Allergic mechanisms must be considered, as the sensitivity may be produced at any time during the course of treatment, after the inadvertent escape of the drug into the subcutaneous tissues as mentioned previously.

Prophylaxis.—Stokes [29] expressed the belief that current conceptions as to the rarity of these complications would probably require modification if periodic examinations of the blood were made. In two of the cases reported here, intensive treatment continued long after signs of anemia appeared and even after the appearance of purpura, bleeding from the gums, weakness and prostration. Warnings of injury to the hemopoietic system are indicated by: history of hemophilia, anemia or hemorrhages or evidence of abnormal general reactions (nitritoid or gastrointestinal), pallor, weakness, purpuric spots and unexplained bruises, bleeding gums, subconjunctival hemorrhages, epistaxis, hematemesis, black stools, stomatitis with fetor, gangrene and decrease in the count of the various elements of the blood. Determination of the icterus index, the Van den Bergh test and patch tests are also of value at the beginning and during the course of treatment.

Treament.—Once the bone marrow has been depressed to the aplastic state, the only hope lies in tiding the patient over until the bone marrow recovers. McCarthy and Wilson found that blood trans-

33. Wheelihan, R. Y.: Granulocytic Aplasia of the Bone Marrow Following the Use of Arsenic, Am. J. Dis. Child. **35**:1032 (June) 1928.

34. Mu, J. W.: Effects of Neoarsphenamine on the Number of Blood Platelets, Proc. Soc. Exper. Biol. & Med. **26**:407 (March) 1929.

35. Smith, C. M.: Severe Bleeding and Purpura Following the Administration of Neoarsphenamine, Arch. Dermat. & Syph. **11**:237 (Feb.) 1925.

fusion is the most valuable measure in the treatment and thought it of life-saving value in three cases. Stokes [29] expressed the opinion that transfusion may be the starting point for unfavorable reactions, except after the second day, when they are definitely valuable. Knott [21] reported a case in which recovery followed fifty-two blood transfusions. The patient later died of pneumonia. Calcium and other hemostatic preparations were used but apparently with little benefit. Sodium thiosulfate has been recommended, but the damage has apparently been done, so that this is of little avail. In accordance with a suggestion that aplastic anemia may be connected with thyroid insufficiency or damage, thyroid extract was also used. Pentnucleotide was given, in the hope of stimulating the bone marrow. Liver preparations were given orally and intramuscularly, a potent preparation being used (1 ampule of 3 cc. being equivalent to 4,800 Gm. of whole liver and capable of producing a complete remission in pernicious anemia in two or three doses), but to no avail, as no evidence of regeneration of the bone marrow could be observed. Cevitamic acid, 50 mg. per day, was given orally, to overcome a possible deficiency in vitamin C as well as for possible desensitization. Whole bone marrow was given orally. Iron and hydrochloric acid were used orally. Potent vitamin preparations were administered to supply adequate amounts of vitamins A, B and D, but these, too, failed to retard the exhaustion of the bone marrow.

SUMMARY

Three cases of severe damage to the bone marrow following treatment with arsphenamine are reported. In all three cases there were marked anemia, granulocytopenia, thrombopenia and a hemorrhagic diathesis. Prolonged bleeding time was noted in two cases. Stomatitis and bleeding from the gums were present in all three. Arsenic was demonstrated in the hair and the nails of one patient and was not present in the other two. Arsenic was found to have been stored in large amounts in the liver and the kidneys of both patients that came to autopsy. In case 3 the patient received but four injections of neoarsphenamine (dosage unknown), so that little arsenic apparently had been injected.

It is to be noted that two of the three patients received intensive antisyphilitic therapy, so that the allergic factor can be ruled out, unless the patient may be considered to have suddenly acquired a sensitivity to the drug used or unless some of the drug accidentally escaped into the subcutaneous tissues. In the other case, an allergic factor is more likely.

In case 1 there was apparent disagreement between the findings on sternal puncture and those at autopsy. Sternal puncture showed few

cells (lymphocytes and normoblasts), while sections of the bone marrow of the femur at autopsy showed a cellularity of between 45 and 85 per cent, of which 18 per cent were normoblasts and 43 per cent lymphocytes. This discrepancy can be reconciled, because in the performance of the sternal aspiration it is possible that the needle may have entered one of the blood spaces rather than the bone marrow itself.

The importance of careful observation of the blood during the treatment of syphilis can be readily understood in the light of present knowledge of the toxicity of the arsphenamines.

Dr. R. H. Jaffé supervised the preparation of and edited this manuscript.

TREATMENT OF CHRONIC DERMATITIS BY A CATAPHORETIC METHOD

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The therapeutic problem presented by dermatitis resulting from long exposure to substances to which the skin is sensitized is often baffling. Such dermatoses are frequently due to chemicals encountered in industry, but entirely similar lesions are caused by irritants not connected with the patient's occupation. In cases of the former type it is not always possible for a patient to change his occupation to protect himself, and when the sensitizing substance is a common one, such as soap, prevention of repeated exposure and cure by such protection are often impossible. Even when the patient can avoid the chemical which initiated the dermatitis, the process often continues obstinately, probably because of secondary sensitization to other substances or secondary infection. Whatever the cause, treatment is often ineffective. For this reason it seems worth while to describe a method which has brought prompt and sometimes long-standing relief to a number of patients, in the hope that it may find application in the numerous cases of occupational dermatitis.

The work reported was begun with a different objective in mind. Cataphoresis has been used for many therapeutic purposes, including the introduction of antiseptic ions into the skin.[1] In the hope that it might produce an effective penetration of fungicides, an attempt was made to treat dermatophytosis by this method. Because the effects seemed better when the chemicals were used in high dilutions, treatment with distilled and tap water without the addition of any antiseptic was tried. Striking benefit was observed in certain cases in which no fungi had been demonstrated and which were probably instances of chronic dermatitis venenata. On account of this fortuitous success treatment by cataphoresis with tap water was introduced in a series of such cases,

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1. Oliver, E. L.: Treatment of Pruritus Ani by Electric Ionization, Arch. Dermat. & Syph. **14**:560 (Nov.) 1926. Shaffer, L. W.: Ionic Medication in Dermatology: Principles, Experimental Confirmation and Clinical Application, ibid. **23**:287 (Feb.) 1931.

with the results here reported. A typical analysis of the tap water was furnished us by the New York City Bureau of Water Supplies:

Croton Water Supply (Parts per Million)

Silicon dioxide (SiO_2)	6.2	Sodium (Na)	3.3	Sulfate (SO_4)	17.0
Iron (Fe)	0.2	Potassium (K)	1.3	Chloride (Cl)	4.0
Calcium (Ca)	13.0	Carbonate (CO_3)	0.0	Nitrate (NO_3)	1.3
Magnesium (Mg)	4.5	Bicarbonate (HCO_3)	42.0	Total solids (180 C.)	73.0

More recently sea water has been used in a few cases of the same type.

TECHNIC

The general technic of therapeutic cataphoresis is described in a number of textbooks.[2] The procedure used by me was simple. For treatment of hands two glass solution trays 12 by 7 by 3 inches (30.5 by 17.8 by 7.6 cm.) were filled with tap water. In a corner of each vessel was placed a thin copper plate about 4 inches (10 cm.) square, one connected by wire to the positive and the other to the negative pole of a source of galvanic current. One hand was placed in each bath and the current turned on to about 5 milliamperes and slowly increased to 15 or 20 milliamperes, being kept, however, below the point at which it caused any burning sensation. Treatment was continued for from twenty to thirty minutes and was repeated at weekly intervals or in some cases three times a week.

In treatment of the forearms or feet larger glass jars were used, and parts not completely immersed were covered with cotton, which acted as a wick. The substitution of pads wet with tap water for baths did not seem to give satisfactory results. When the hands and the forearms were immersed, the current could usually be increased to 40 milliamperes without discomfort. Little difference could be noted between the effect of the positive and that of the negative bath. Occasionally the patient complained of more discomfort in one than in the other, more often in the positive bath.

In the earlier treatments a 45 volt dry battery of the type used in radio sets was used. A milliampere meter and a variable resistance were interposed between the battery and one of the terminals, and a voltmeter with a switch was connected across the terminals. Later the voltage was stepped up to 90 and then to 135 volts by arranging batteries in series. It is more convenient to use a small transformer with a rectifying tube and suitable condensers (fig. 1). This delivers a maximum electromotive force of 90 volts when attached to a 110 volt alternating current wall socket. It is essential to have apparatus of an adequate voltage which will not deliver a dangerous current in case the patient comes in contact with the electrodes.

RESULTS IN CHRONIC DERMATITIS

The most striking results were obtained in twenty patients with chronic dermatitis of the hands. Eight were male and twelve female, and their ages ranged from 7 to 61 years. Ten were engaged in housework; two were waiters, two waitresses, one a bartender, one a window

2. Leduc, S.: Electric Ions and Their Use in Medicine, translated by R. W. MacKenna, London, Rebman, 1913. Jones, H. Lewis: Medical Electricity, ed. 8, London, H. K. Lewis & Co., 1920. Friel, A. R.: Electric Ionization, Baltimore, William Wood & Company, 1920.

cleaner, one a milliner, one a keeper of a morgue and one a pathologist; two had no definite occupation. All had suffered from dermatitis either intermittently or continuously for from six months to nineteen years, and the eruption had been active for a month or more before treatment was started in all cases. In appearance the patients showed the

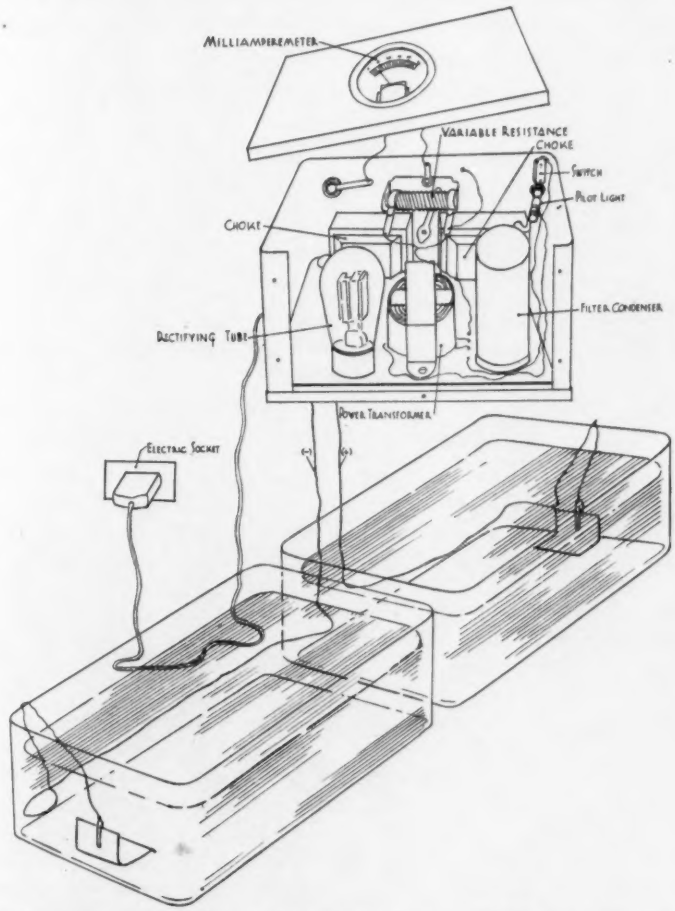

Fig. 1.—Apparatus for the reduction and the control of the current.

variations which are familiar in occupational dermatitis. All except two with palmar eruptions showed lesions on the backs of the hands. In a number both the backs and the palms were involved. Practically all showed active vesiculation or the remains of vesicles, but a few showed only dry, red, scaling and fissured skin at the time of treatment. A number showed pustules, edema and other evidence of pyogenic infection. Most of the patients were examined for fungi, and in none were they found. A reaction to solution of formaldehyde by patch test was

obtained in the case of the keeper of the morgue, and the pathologist suspected solution of formaldehyde as the cause of his eruption. In most instances soap was suspected to be the cause of the dermatitis, though the etiologic diagnosis was not well established. All the patients had been treated with salves or wet dressings without lasting relief. Sixteen had had roentgen therapy, in most instances with temporary relief, but it is interesting that in two patients whom this treatment had not helped the condition cleared under treatment with cataphoresis. Two patients said that they had been given forty or fifty roentgen treatments, and in the cases of a number who had received much relief from previous roentgen treatments the amount already given made it unwise to continue irradiation.

The rapidity of response was striking. In most cases itching was relieved and the appearance much improved after one or two treatments. Clearing up the last traces of the eruption required a longer time, but in all twenty cases the skin became practically normal. Two patients experienced relapse while under observation, but the condition again cleared after two or three treatments.

REPORT OF CASES

CASE 1.—The keeper of a morgue, aged 46 years, had suffered from a distressing pruritic dermatitis intermittently for over seven years. His only relief had been from roentgen irradiation, which would cause the eruption to disappear for a few months, but he had received a total of 3,200 roentgens. The skin of the forearms and the backs of the hands was diffusely red and thickened. There were numerous excoriations and patches of crusted, weeping and pustular dermatitis. A patch test with solution of formaldehyde (1 per cent dilution) gave positive results. After six weekly treatments by cataphoresis with tap water the eruption completely disappeared, and it remained clear for a year, after which there was a local recurrence on the left hand. The patient said that he wore rubber gloves and protected himself as much as possible from solution of formaldehyde, but such procedures had not availed before in preventing a prompt relapse.

CASE 2.—A housewife aged 22 presented a diffuse dermatitis involving the entire hands except for small patches of normal skin on the palmar side of one thumb and of each index finger (fig. 2). The skin was edematous and thickly studded with minute vesicles. There was much maceration of the skin on the fingers, and extensive desquamation was present on the palms. The hands were deeply stained by potassium permanganate in wet dressings. Examination for fungi gave negative results. The dermatitis had been present four years. The patient had received ultraviolet and roentgen (400 r) irradiation; salves had been administered, at times with improvement, but during the whole period the skin had never appeared normal. With cataphoresis there was improvement after the first treatment, and after thirteen treatments in two months the hands appeared normal. The patient was observed after eight months, and at that time there had been no relapse.

CASE 3.—A woman aged 28 gave a history of recurrent dermatitis, at times on the neck or the flexures of the elbows and at times on the hands, for ten years. About two years before admission she began work as a waitress, and the eruption

on the hands soon became persistent. It cleared after nine roentgen treatments at another clinic but recurred in three or four months. She gave up work for one summer and the skin healed, but there was a relapse on her return to work.

The entire skin of the hands was reddened, dry and hyperkeratotic. In areas there were remains of many dried vesicles and in other areas marked desquamation and some fissures. After one or two treatments by cataphoresis with distilled water there was marked improvement, but some irritation and desquamation per-

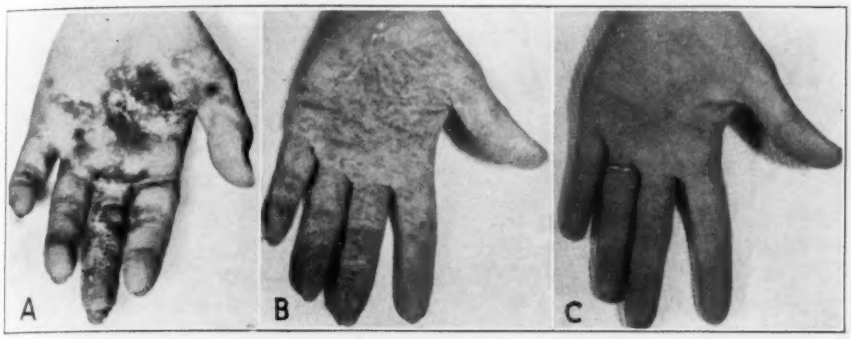

Fig. 2 (case 2).—*A*, April 3, 1936, before treatment; *B*, April 24, 1936, showing improvement after three treatments; *C*, March 1, 1937, showing persistence of the cure eight months after the end of the treatment.

Fig. 3 (case 11).—Severe vesiculopustular dermatitis of both hands of one year's duration in a boy aged 7 years. *A*, Nov. 18, 1936, before treatment; *B*, Feb. 11, 1937, showing practically complete clearing after nine treatments; *C*, March 15, 1937, showing persistence of the cure one month after the last treatment.

sisted for three months, during which she received twelve such treatments. With the change from distilled water to tap water there was prompt improvement; after nine such treatments the hands appeared normal and the patient returned to work. Six months later some scaliness developed on the fingers. This disappeared after three more treatments.

Such results are difficult to evaluate because dermatitis so often clears of itself if the skin is protected. In all these cases, however, the condition was of long standing and had resisted other forms of treatment. It seems probable that the cataphoresis was responsible for their cure. It seems even more significant that in the three cases described and the six others listed in the table, which were observed for some time after treatment, cure persisted for a long period. This had not been the experience of the patients when relieved by roentgen irradiation or other methods.

Patients Treated by Cataphoresis and Followed After Recovery

Patient	Sex and Age, Yr.	Occupation	Duration of Intermittent Dermatitis, Yr.	Number of Treatments	Duration of Treatments	Period of Observation After Treatment	Result
1	M 46	Keeper of morgue	7½	6	5 wk.	14 mo.	Hands remained clear for a year; now a few patches on left hand
2	F 22	Housewife	4	13	2 mo.	8 mo.	Hands remained clear
3	F 28	Waitress	10	21	6 mo.	6 mo.	Cleared; slight relapse after 6 mo.; response to two additional treatments
4	M 38	Pathologist	19	4	3 mo.	20 mo.	Cleared; slight relapses; response to application of ointment
5	M 48	Waiter	10	12	4 mo.	2 yr.	Hands remained clear
6	F 19	Housewife	8	3	2 wk.	20 mo.	Practically normal; hands have given no trouble since
7	F 29	Housewife	2	5	4 mo	10 mo.	Report by letter "hands are all right"
8	M 61	None	8	4	2 wk.	1 yr.	Remained clear (wet dressings with solution of aluminum acetate, N. F., also used)
9	F 29	Housewife	21	6	5 wk.	13 mo.	Cleared; recurrence after 10 mo.; remained clear for 6 wk. after 3 more treatments
10	F 35	Housewife	15	7	6 wk.	15 mo.	Cleared 10 days after last treatment and clear since; first winter in 15 years that hands remained clear
11	M 7	Schoolboy	1	11	3 mo.	1 mo.	Clear at last observation, 1 mo. after end of treatment

Similar benefit was obtained by a patient with a vesicular and bullous dermatitis of the feet and legs which had been present for over a year. In a number of cases acute dermatitis cleared promptly, but in them there was a distinct possibility of spontaneous cure. There were other cases of chronic dermatitis in which there was no response, mostly those in which fungi were found or their presence was suspected on clinical grounds.

RESULTS IN DERMATOMYCOSES

In ten cases of dermatophytosis and nine cases of moniliasis in which the diagnosis was established by microscopic and cultural examination, from two to ninety-one treatments by cataphoresis were given.

Various fungicides, sodium hypochlorite, potassium iodide, compound solution of iodine U. S. P., sodium borate, salicylic acid, sodium benzoate and potassium permanganate were tried in the negative bath, and mercury, copper, zinc, methylrosaniline (gentian violet) and aniline green in the positive bath. In five of these cases treatment with tap water was also employed. A few patients showed some clinical improvement, but even in those most persistently treated, fungi could still be found at the end of the course. So far as one can judge from this experience, the method is of no value in dermatomycoses.

COMMENT

It is impossible to state why the electric current benefited these eruptions. There are several possibilities. In the first place, the ions contained in the dilute solutions were doubtless introduced during the treatment and may have had some beneficial effect. All these ions are, however, present in the skin in traces, and sodium, potassium, calcium and chloride are present in much larger amounts than any which could be introduced by such a method.

A second possibility is that toxic ions were removed by the electric current, either out into the surrounding bath or into the circulation, but in either case eliminated from the skin. Bordier reported that he found uric acid in the baths after treating the arms of gouty patients with cataphoresis. When my patients were treated with distilled water or tap water the chloride content of the anode bath after cataphoresis was usually higher than that of the cathode bath. The differences were, however, slight, from 3 to 5.9 mg. in a bath containing a hand or a foot, and it was probable that chloride in such amounts might have come from the cutaneous surface.

In an effort to detect the removal of toxic ions, two experiments were performed: In one, a patient with an arsphenamine eruption, whose blood contained 0.3 mg. of arsenic per hundred grams of dry blood and who had an involvement of the hands, was given two treatments of one hour with tap water with a current of from 15 to 20 milliamperes (90 to 135 volts). Arsenic may act as either an anion or a cation, and both the baths after the treatment were examined for arsenic. A trace of arsenic could be found in both the positive and the negative bath, which seemed inconclusive. Another patient with a phenolphthalein eruption involving the hands was similarly treated with a current of from 20 to 50 milliamperes for one hour. After treatment the two baths showed no color on addition of alkali, but after being concentrated to a small volume, a faint pink was observed in the anode bath. It seemed that in this instance phenolphthalein was carried from the tissues toward the positive pole by the current. As to whether

there was a similar extraction of the foreign ions which caused the dermatitis in my other cases, there is no evidence.[3]

It seems more probable that the therapeutic effect was due neither to the introduction nor to the removal of ions. Levant,[4] who treated arthritis by cataphoresis with sodium salicylate and other chemicals, found his results equally good if he used tap water. The application of an electric current to a solution causes the migration toward one or the other pole not only of ions but of colloids and particles in suspension, such as bacteria and blood cells. Furthermore, a current alters the permeability of membranes placed between the poles and causes water and nonionized substances in solution to pass through them (electro-osmosis).[5] These processes probably played roles in producing the effects I have reported, but an explanation of these effects on this basis would as yet be hypothetical. There is, however, an analogy between the cataphoretic method and roentgen irradiation, the beneficial effects of both on inflamed tissues being unexplained. An understanding of the process under discussion must await more knowledge of electrokinetic phenomena in normal and diseased cells.

SUMMARY

Chronic dermatitis of the hands and feet, probably due to contact sensitization, was treated with a galvanic current, the involved parts being immersed in tap water or sea water. Striking improvement occurred after one or two treatments in most cases. In ten patients who were treated consistently and followed after treatment was stopped, the eruptions disappeared, and in six they have not recurred. No explanation can be offered as to why this treatment was beneficial. Attempts to treat dermatophytosis and moniliasis by cataphoresis with various fungicides were unsuccessful.

57 West Fifty-Seventh Street.

3. Dr. E. M. Maechling made the determinations reported.

4. Levant, Harry L.: The Use of Iontophoresis, Arch. Phys. Therapy **16**: 552 (Sept.) 1935.

5. Abramson, H. A.: Electrokinetic Phenomena and Their Application to Biology and Medicine, New York, Chemical Catalog Company, 1934.

SYPHILITIC ASTHMA WITH ATROPHIC CIRRHOSIS IN ACQUIRED SYPHILIS

REPORT OF A CASE

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Syphilitic bronchial asthma is apparently one of the most unusual manifestations of syphilis. A search of the literature showed but two cases, one reported by Sézary and Alibert [1] and the other by Joltrain.[2] Atrophic cirrhosis, on the other hand, does not seem to be an unusual occurrence in connection with syphilis. The association of syphilitic asthma with atrophic cirrhosis in the same patient has received no consideration in the literature. The importance of this association will be realized when it is recalled that arsenicals may be markedly beneficial to asthma but exceedingly harmful to cirrhosis. Furthermore, it should be emphasized that the asthmatic state possibly may render the liver more susceptible to shock from arsenical administration, as in the case which I shall now describe.

REPORT OF CASE

On May 12, 1924, a well developed man aged 30 and weighing 155 pounds (70 Kg.) noticed a syphilitic chancre on his penis. At this time, excepting his syphilis, examination of the patient disclosed nothing of interest other than a muddy complexion suggesting hepatic disease. He stated that two brothers had died from what was thought to be cirrhosis of the liver. Antisyphilitic treatment was instituted, and the patient received forty-six injections of varied arsenicals and sixty injections of bismuth subsalicylate in a continuous system of treatment, with oral administration of potassium iodide and mercury rubs during intervals of three weeks between courses of arsenic and bismuth subsalicylate.

On Nov. 5, 1927, the Wassermann reaction was strongly positive, but the patient disclosed no other evidence of disease. The spinal fluid was normal. There was no evidence of visceral, cardiovascular, osseous or neural syphilis. Bromsulphalein and galactose tolerance tests revealed no hepatic damage. Since the patient seemed perfectly well, he was placed under observation without further antisyphilitic therapy.

Up to Dec. 26, 1928, there was no evidence of disease other than a strongly positive Wassermann reaction. On this date mild jaundice developed and continued over three weeks. There were no other symptoms. The patient felt well.

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1. Sézary, A., and Alibert, J.: Syphilitic Asthma, Bull. et mém. Soc. méd. d. hôp. de Paris **46**:242-250 (Feb. 3) 1922.

2. Joltrain, E.: Asthma and Syphilis, Bull. Acad. roy. de méd. de Belgique **6**: 12-19 (Jan.) 1931.

The liver was not enlarged or tender. There was no gastrointestinal disturbance. The temperature, pulse and respiration were normal. The blood pressure was 118 systolic and 67 diastolic. Tests of hepatic function showed an excretion of galactose of 6.5 Gm., 110 mg. of bilirubin per liter of serum, an icteric index of 69 and 40 per cent retention of bromsulphalein. The blood count revealed 7,000 white cells, with 10 per cent eosinophils, 4,750,000 red cells and 88 per cent hemoglobin. The Wassermann reaction was strongly positive. The urine showed no sugar, albumin or tyrosine, but much bile was present.

By Jan. 17, 1929, the jaundice had cleared, and tests of hepatic function disclosed no evidence of disease, but during the next four days severe bronchitis developed, accompanied with periodic attacks of dyspnea. These dyspneic attacks were followed by coughing and expectoration of viscid mucus containing eosinophils. A concert of sibilant and sonorous rales was heard over the lungs. In every respect these dyspneic attacks resembled those of bronchial asthma, although the patient had never previously suffered from bronchial asthma and there was no history of allergic disease in the family.

The bronchitis and asthma became more severe. The temperature and the pulse remained normal. Repeated examinations of sputum disclosed no tubercle bacilli. Specific desensitization, administration of bacterial vaccines, nonspecific proteins, calcium and viosterol, iodides and endocrine products, roentgen irradiation, a ketogenic diet, hydrotherapy and massage, ultraviolet irradiation and fever therapy were employed, but there was no improvement. Injection of epinephrine, and use of stramonium cigarets and capsules of amytal and ephedrine afforded temporary relief.

In view of the positive Wassermann reaction and a roentgenogram suggestive of pulmonary syphilis, mercury rubs, iodides by mouth and bismuth subsalicylate intramuscularly were used, but these produced no benefit. Since the few scattered reports in the literature of pulmonary syphilis and syphilitic asthma called attention to the decided improvement obtainable from the arsenicals, it was decided after careful clinical study and tests of hepatic function to administer neoarsphenamine. After the first injection the patient noted improvement, and by the time the sixth injection was given, recovery was complete. A roentgenogram of the lungs at this time showed that the shadows suggesting pulmonary syphilis had disappeared. Bromsulphalein and galactose tolerance tests and a determination of the icteric index revealed no hepatic damage. The Wassermann reaction, however, continued to be strongly positive. The patient was advised to continue with a short course of treatment with an arsenical and with a bismuth preparation, followed by ingestion of iodides and mercury rubs, before a rest period, but he felt so well that he considered further treatment unnecessary.

Up to Jan. 3, 1937, there were six recurrences of bronchitis and asthma. In each of these attacks from three to five injections of neoarsphenamine brought prompt relief, while iodides, mercury and bismuth preparations seemed ineffective. Because of his muddy complexion, his family history and the jaundice in 1928, the liver was carefully watched. Except during the attack of jaundice, the patient never manifested any significant change in the bromsulphalein, the galactose tolerance or the urobilinogen test for hepatic disturbance or in the icteric index. The important signs and symptoms of Laënnec's cirrhosis, such as enlargement of the liver, enlargement of the spleen, weakness, abdominal pain, tenderness over the liver, gastrointestinal upset with flatulence or hemorrhage, loss of weight, transient edema of the ankles, visible collateral circulation and anemia, were never

present; nor were there evidences of visceral, cardiovascular, osseous or neural syphilis, although the Wassermann reaction remained strongly positive. Except for bronchitis and asthma, the patient always felt well and able to do hard work.

On Jan. 3, 1937, the patient had another of his attacks. One injection of neoarsphenamine was followed by marked improvement. However, two days after the administration of the second dose the conspicuous signs and symptoms of severe hepatic damage developed, with deep jaundice, nausea and vomiting, belching, flatulence, abdominal tenderness especially marked over the liver, palpable liver and spleen and lethargy alternating with restlessness and semiconsciousness. The temperature, pulse and respiration were normal. The blood pressure was 120 systolic and 70 diastolic. The van den Bergh reaction was biphasic. Tests of hepatic function showed an excretion of galactose of 7 Gm., 230 mg. of bilirubin per liter of serum, an icteric index of 160 and a 100 per cent retention of bromsulphalein. The blood count revealed 6,400 white cells, with 7 per cent eosinophils, 4,480,000 red cells and 85 per cent hemoglobin. The Wassermann reaction was strongly positive. The urine showed no sugar, albumin or tyrosine, but there was urobilinogen. In spite of a high carbohydrate diet and continuous intravenous administration of dextrose, the patient lapsed into coma and died January 12.

Autopsy showed a liver weighing 1,600 Gm. and presenting the picture of a Laënnec's cirrhosis, with conspicuous evidences of superimposed acute toxic injury. The lungs revealed chronic bronchitis, and there were many pleural adhesions. The spleen weighed 400 Gm. and showed histologic evidence of chronic passive congestion. There was no ascites.

COMMENT

The risk of producing toxic hepatitis by arsenical medication in the presence of a damaged liver has long been known. In reviewing the literature on syphilis of the liver, atrophic cirrhosis and toxic hepatitis due to arsenicals, I was surprised at the paucity of completed reports dealing with these forms of destructive hepatic disease. I was unable to find a single report in which sudden death followed administration of an arsenical to a patient with atrophic cirrhosis of the liver.

It is well recognized that extensive hepatic injury may be present without any clinical or laboratory evidence of such injury. However, when a careful clinical examination and tests of hepatic function, especially the bromsulphalein, the urobilinogen and the galactose tolerance test are performed and the icteric index is determined, there is less likelihood of the appearance of fatal hepatic damage from unjustified administration of arsenicals. Yet these facts must not be neglected: that early atrophic cirrhosis in the majority of instances produces little or no evidence of its presence and that its presence is discovered for the most part accidentally at autopsy.

In my patient the development of bronchial asthma during an attack of jaundice suggests that the hepatic damage may have been the inciting influence. A search of the literature, however, disclosed no report in which hepatic damage was regarded as the initiating influence for attacks of bronchial asthma.

Little mention has been made in medical writings of syphilis and its relation to asthma. Ramirez and St. George [3] in a study of the incidence of syphilis in bronchial asthma concluded that syphilis is not a cause of true asthma and that syphilis is not notably present among asthmatic patients. Hecht [4] reported a low incidence of syphilis among asthmatic patients.

In the cases of syphilitic asthma reported by Sézary and Alibert and by Joltrain prompt relief followed the administration of arsenicals. Fraenkel [5] spoke highly of the results which can be obtained in syphilitic bronchitis with associated asthma, and he recommended the use of arsphenamine at the outset of treatment. The great danger, on the other hand, attending such medication is well illustrated in my case. Truly striking improvement may follow arsenical medication, but asthmatic patients are notorious for their unpredictable shock reactions to parenteral medication. This danger should be kept in mind when arsenical medication is considered for the patient suffering from syphilitic asthma, especially when there exists the possibility of visceral or hepatic damage.

SUMMARY

Syphilitic asthma developed during an attack of jaundice in a patient with clinically unrecognizable atrophic cirrhosis of the liver. Arsenical medication produced striking relief of the asthma, at the expense of creating rapidly fatal toxic hepatitis. Attention is directed toward the danger of inducing fatal shock by administration of arsenicals to patients with syphilitic asthma.

546 West Market Street.

3. Ramirez, M., and St. George, A.: The Incidence of Syphilis in Bronchial Asthma, Am. J. Syph. **11**:59-65 (Jan.) 1927.

4. Hecht, R.: The Wassermann Reaction in Asthma, Illinois M. J. **59**:366-368 (May) 1931.

5. Fraenkel, A.: Syphilis der Brustorgane, Berlin, Julius Springer, 1923, pp. 84-90.

SCLEREDEMA ADULTORUM (BUSCHKE)

ITS RELATION TO TROPHEDEMA AND ITS PATHOGENESIS

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Scleredema adultorum (Buschke) [1] is a rare disease. Only two cases have been reported in the American literature, by Epstein,[2] who termed the condition a "distinct entity that has a definite clinical course and characteristic histopathology." Following is a report of a complete study of a case,[3] including cutaneous capillaroscopy and examination of biopsy material with various stains. There is a controversy in the literature of the world as to whether this disease is a clinical entity. While members of the German school affirm its identity, the French authors doubt or deny it. The latter contend that scleredema is a unique variety of trophedema. I believe that my findings add light to this question, as well as to knowledge of the nature and the pathogenesis of scleredema adultorum.

REPORT OF A CASE

R. G., a housewife aged 37, came to the clinic complaining of stiffness of her face, chest, neck, and upper extremities and shooting pains in her arms, her forearms and the back of her neck. These attacks occurred intermittently and lasted for from one half to six hours. She said that she always felt cold, even feeling "cool" when others complained of severe heat. She hardly ever perspired, and on the day of her initial examination the patient said that she felt comfortably cool, when the temperature was 87 F.

The patient stated that her complaints began seven months before, three months after the birth of twins but said "people have remarked long ago that I have a stiff-looking face."

She was born in the city of New York, had a normal birth and was breast fed up to the age of 24 months. She had abscesses on her neck and in her left groin when 1 year old. She had chickenpox at 18 months and was sick for two weeks. She had measles at 6 years and was confined to bed for ten days. During this illness she had one major convulsion. She underwent tonsillectomy at 6 years of age.

From the Neurologic Clinic of the New York Post-Graduate Medical School and Hospital.

1. Buschke, A.: Ueber Scleroedem, Berl. klin. Wchnschr. **39**:955, 1902.
2. Epstein, N.: Scleredema Adultorum, J. A. M. A. **99**:820 (Sept. 3) 1932.
3. The condition in this case was diagnosed as scleredema adultorum (Buschke) in the Skin Clinic of the New York Post-Graduate Medical School and Hospital.

The patient began school at 7 and was graduated at 14. She was considered an average pupil; she had many friends and got along well with her teachers. She attended business school for one year, after which she obtained a position as a bookkeeper and worked steadily. She was sociable and popular, liked dancing and disliked being alone. She married after a two year courtship, at 21 years; her husband was her first cousin. She gave no history of miscarriages; she had three children, two of whom were twins aged 9 months. She began to menstruate at 11 years of age, her periods occurring at twenty-eight day intervals and lasting two and a half days. On the first day she had only slight staining, and there was hardly any flow on the second day.

The father and the mother of the patient were supposed to have been treated for syphilis when she was 7 years of age. The patient's Wassermann reaction at that time was negative. The patient's mother, father and two sisters all had diabetes.

Her habits were normal and regular. She abstained from alcohol but smoked twenty cigarets per day. Her weight was 140 pounds (52.3 Kg.), and it was necessary to adhere to a diet to retain this weight.

Physical and Neurologic Examination.—The patient was of medium size and well nourished. She looked somewhat rigid and anxious and had a masklike facies. Her gait was normal, and the associated movements of both upper extremities were present, equal and within normal limits. All the cranial nerves were normal. The superficial as well as the deep reflexes were normal. There were no pathologic reflexes. A careful sensory examination for all modalities showed no deviation from normal findings. Physical examination, including that of the vagina and of the rectum disclosed no abnormality. The skin of her face, neck and shoulders and to a lesser extent of the abdomen and the lower extremities appeared pale, tense and somewhat shiny. The skin and subcutaneous tissue felt like one solid mass of boardlike consistency; it could not be pitted or wrinkled. There was no marked dermographia, though Sergent's line spread about 3 cm. and remained visible for about two minutes. The patient did not complain of pain on deep pressure but did notice spontaneous pain over the posterior aspects of both shoulders, radiating down to both arms.

Complete serologic examination, including Wassermann tests of the blood and the spinal fluid, showed normal findings. Urinalysis showed no albumin, sugar or casts. Chemical examination of the blood showed 10.1 mg. of calcium, 26 mg. of cholesterol, 80 mg. of sugar and 28 mg. of nonprotein nitrogen per hundred cubic centimeters. The basal metabolic rate was —13 per cent. Capillary studies with a binocular Zeiss capillaroscope showed most of the capillaries to be of normal size and caliber, but there were a few which showed marked dilatation of the first loop crossing as well as a tendency to tortuosity. These changes closely resembled those in early Raynaud's disease. Roentgenograms of selected areas of the upper and lower extremities revealed no gross abnormality of either the osseous structures or the soft tissues, though the muscle bellies appeared rather prominent and dense. There was no evidence of fibrofascial thickening or abnormal calcification. Electric reactions revealed no abnormality.

Pathologic Picture.—A biopsy specimen was removed from the right side of the neck and the tissue stained with methylene blue and thionine and by the hematoxylin-eosin method and the methods of Van Gieson, Spielmeyer, Weigert and Pal, Bielschowsky, Cajal and Hortega. The entire material was studied in serial sections.

The epidermis was little changed, except that some of the cells seemed to be thicker, with enlarged and somewhat paler nuclei. The rete pegs were definitely

prolonged and widened. The papillae were elongated. The vessels were dilated but not filled with blood. There were no infiltrations around the blood vessels; the walls of the vessels appeared somewhat thicker than normal, but this was due not to any proliferation of cells but to a swelling of the endothelial and adventitial cells. Under higher magnification, these cells were shown to contain vacuoles filled with amorphous material that stained reddish by Van Gieson's method, bluish by Spielmeyer's and light brown in silver and remained colorless in hematoxylin and eosin. These vacuoles could be followed through the wall of the vessel from the lumen to the periphery of the vessel.

The connective tissue cells were definitely increased throughout the cutis. These were not in group formation but diffusely spread in the tissue. The nuclei of the cells were enlarged and contained less chromatin than normal; the body plasma was more prominent and distinct. The characteristic and unmistakable indication of the disease was the marked hypertrophy of the collagen fibers. These were many times greater than normal by actual measurement. They were separated irregularly by an edematous substance which stained the same as the vacuoles in the walls of the vessels. The entire tissue looked like a coarsely fenestrated network with the collagen fibers assuming various sizes and shapes.

The elastic fibers were not increased, although some appeared torn or split, especially in an edematous area.

The Spielmeyer and Weigert-Pal stains revealed evidence of disintegration of myelin. The longitudinal-coursing nerve presented areas of loss of myelin, and under higher magnification one could observe coarse fibers and clumps of myelin débris. At some places the network of the myelin sheath was plainly seen to be irregularly broken and its meshwork or funnel-shaped structure disorganized and obviously defective. When the nerve was followed in serial sections toward its termination it was seen to be fading out into its terminal arborization and at some places fused with a pool of light-staining and amorphous substance which infiltrated the fibers of the corium as well as the muscle fibers. The same blue-violet substance was present in a few muscle spindles which were present in the preparation. These appeared swollen, and the connective tissue capsule surrounding each muscle spindle was divided and contained a large space filled with this fluid.

In the silver preparations some of the axon cylinders appeared ballooned and inflated, split and crumpled. This was noted especially in the nerves of the subcorium.

COMMENT

In order to comment in accordance with scientific principles, it is well to review the established pathophysiologic data on edema. By edema is meant an abnormal accumulation of fluid in the intercellular tissue spaces. The fluid in these spaces is not exactly the same as lymph, although the lymphatic system includes the tissue spaces. This is due to the fact that the lymph vessels, like the blood vessels, represent a closed system, and the fluid does not come into actual contact with the tissue cells. Exceptions to this may be found in the liver and the spleen. At other points the endothelial cells act as a barrier membrane, bringing nutritive material too, and removing metabolites from, the tissue.

Although tissue fluid is similar to lymph, its exact composition is not known, and its source has been the subject of controversy. It is likely that the tissue fluid is derived from the blood and is moved

partly back into the blood stream and partly into the lymphatics. Its formation and removal are governed by various forces, such as filtration, properties of the endothelial membranes, diffusion and osmotic pressure of the blood as well as of the tissue spaces. Normally there is a harmonious interplay of these forces, producing a constancy of tissue reservoirs. In edema, however, there is a disturbance of the equilibrium of the formation and return of the fluid, resulting in an increase of tissue fluid in the intercellular spaces.

Edema may occur physiologically in muscle during and some hours after activity. Pathologically it may be due to (1) venous obstruction, (2) cardiac edema, (3) renal edema or (4) abnormal permeability of the capillary wall. There was no indication in the case reported here of any involvement coming in the first three categories, but close scrutiny will divulge, as will be seen later, that there was a disturbance in the coefficient of permeability of the capillary wall.

It may be well to point out that when the capillary is severely damaged, no edema results, for in that case the entire plasma and the colloids of the blood filter out. The blood corpuscles then accumulate in the vessels in clumps, finally obliterating the lumens so that no fluid can pass; only when part of the proteins and colloids escape into the tissue is the osmotic balance disturbed in such a way that edema results.

That there exists a functional disturbance of the capillaries may be safely claimed from various observations in my pathologic studies. Though the capillaries and the arterioles did not show any structural change, they were all dilated and presented marked evidence of vasostasis. This would act as an underlying cause for the physiologic dysfunction of the wall of the vessel and produce a disturbed permeability leading to excessive fluid in the tissue spaces.

An important observation in the biopsy studies was the degeneration present in the peripheral nerves. This is essential in the light of the accepted fact that Rouget cells, which regulate the size of the capillaries, possess tone. This tone varies with nervous influences, and it is generally believed that sympathetic fibers pass to the Rouget cells of the capillary wall. The demyelinization observed in the peripheral fibers could account for the vasostasis, for the sympathetic nerves which supply the wall of the vessel course among the peripheral nerves.

The endothelial cells might have been acted on directly by a histamine-like substance as a result of the production of harmful metabolites following a disturbance of the activity of the tissues. Edema would result in such a case, accompanied with a secondary involvement of the nerve. Indeed such changes have been reported in the peripheral nerves in cardionephritic edema. Such degeneration of a vulnerable nerve fiber would, on the other hand, influence the normal caliber of a vessel and once more aggravate the endothelial barrier

between the various reservoirs of fluid. One might thus construe the process as a vicious circle the degeneration of the nerve ultimately producing edema, and the edema producing degeneration of the nerve. When other factors come into play to establish an equilibrium once more, one observes clinical evidence of a remission.

I do not wish to assign to any specific factor the sole responsibility for this disease, for I believe that any pathologic process is due to a pattern of circumstances and not to a single stimulus. This was true in the present case. One would have to take into consideration the hereditary and constitutional predisposing factors, the vulnerability of the vascular, nervous and endocrine systems and the toxic metabolic and infectious agents. Usually the inadequacy of one system is so dominant as to cause the process to be attributed to it.

This would account for the various factors mentioned as etiologic in the literature of trophedema. Meige [4] expressed the opinion that the disturbance is due to a trophic disorder and assumed a change in the sympathetic tracts of the cord. Garnier and Huguenin [5] attributed the disturbance to an increase of tone in the sympathetic nerves supplying the vascular system. Léri and Péron [6] and Delhaye [7] claimed to have found the cause in changes of the sacral roots in a case of spina bifida accompanied with trophedema of the extremities. Long [8] showed that the connective tissue of the nerve presented marked hypertrophy, and Gordon [9] reported a case of trophedema of cerebral origin. Osler [10] attributed the edema to underlying endocrinopathy; Ayala,[11] Rietti [12] and Nové-Josserand and Laurent [13] accepted this view. Althoff

4. Meige, H.: Trophoedème du membre inférieur droit avec lombo-sciatique droite, Rev. neurol. **21**:571, 1913.

5. Garnier, M., and Huguenin, R.: Un cas de trophoedème acquis: Étude clinique et physiologique avec présentation du malade, Bull. et mém. Soc. méd. d. hôp. de Paris **47**:1192, 1923.

6. Léri, A., and Péron, N.: Le "syndrome" trophoedème: trophoedème nerveux, trophoedème lymphatique, Bull. et mém. Soc. méd. d. hôp. de Paris **47**:1834, 1923.

7. Delhaye, A.: Meiges trophedema bei spinobifida occulta, Nederl. tijdschr. v. geneesk. **5**:688, 1924.

8. Long, E.: Examen histologique des teguments et des troncs nerveux dans un cas de trophoedème congénital, Nouv. iconog. de la Salpêtrière **20**:155, 1907.

9. Gordon, A.: Segmental Trophic Edema of Cerebral Origin, J. Nerv. & Ment. Dis. **66**:381, 1927.

10. Osler, W.: Hereditary Angio-Neurotic Edema, Am. J. M. Sc. **95**:362, 1888.

11. Ayala, G.: Le trophoedème chronique et le système endocrino-sympathique, Encéphale **1**:319, 1913.

12. Rietti, F.: Sul trofoedema cronico di Meige, Policlinico (sez. med.) **31**: 520, 1924.

13. Nové-Josserand, L., and Laurent, C.: Le trophoedème chronique, Gaz. d. hôp. **82**:509, 1909.

described a case of trophedema following ovariectomy, and Sequeira [14] reported a case of trophedema following fracture of the skull.

As already indicated in the introductory paragraph, I believe that scleredema adultorum is not a clinical pathologic entity. Nové-Josserand and Laurent subdivided trophedema into (1) congenital, not hereditary; (2) chronic hereditary, and (3) acquired, not familial, of chronic and trophic origin. Conditions of the third type may occur either in youth or in adulthood. It is this involvement in adulthood which has been generally taken for an independent entity. However, 20 of 41 cases which have been gathered from the literature and reported by Epstein as instances of scleredema adultorum occurred in subjects less than 20 years of age. Fourteen of the patients were less than 10 years of age. One of the two original patients mentioned by Epstein was 16 years of age. Von Graevenitz [15] and Seifert [16] reported the appearance of Buschke's scleredema adultorum in infants and even in new-born babies. Seifert's case involved a boy 6 years of age. On the other hand, it has long been known that trophedema may occur in the adult. Gordon reported such a case in a man 67 years of age, following a probable insult in the supramarginal area, injuring the higher trophic centers.

It has been claimed that scleredema adultorum is a demarcated entity because "it is a self limited disease." It is noteworthy that the chronicity of trophedema is not uniform. In some cases there is a mild course with remissions. This has been emphasized by Gougerot and Mondo,[17] who described the condition in their case as progressive in *Schuben* (thrusts). In one of Epstein's cases which he considered to be one of scleredema adultorum cure was not complete. The severity in the course of symptoms in trophedema may be due to many factors, as in the cases reported by Moniz [18] and Hope and French,[19] in which all the symptoms disappeared during pregnancy. An acute infectious disease may aggravate the condition. Sequeira [14] reported a case of scleredema adultorum following fracture of the skull. Glandular disturbances may have an aggravating effect on the course, as in the case

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14. Sequeira, J.: Report of a Case of Trophedema Following Skull Fracture, Brit. J. Dermat. **26**:323, 1914.

15. von Graevenitz, N.: Ueber 3 Fälle von Sklerödema adultorum Buschke, Monatschr. f. Kinderh. **39**:257, 1928.

16. Seifert, A.: Sklerödem bei einem 6 Jahre alten Kinde, Arch. f. Kinderh. **91**:220 (Sept.) 1930.

17. Gougerot and Mondo, cited by Nicolay, A.: Beitrag zur Tropoedemafrage, Thesis, University of Berlin, 1931.

18. Moniz, E.: Sur le trophoedème chronique de meige; nouveau cas; considérations sur leur étiologie, Rev. neurol. **28**:1086, 1921.

19. Hope, W. B., and French, H.: Persistent Hereditary Edema of the Legs with Acute Exacerbations: Milroy's Disease, Quart. J. Med. **1**:312, 1907-1908.

of Althoff, who described a case of trophedema following ovariectomy. The case reported here showed an increase in symptoms following pregnancy, so that the patient was forced to seek medical aid.

SUMMARY

A case of scleredema adultorum (Buschke) is reported.

Detailed histopathologic studies reveal increase and hypertrophy of collagen fibers, with degeneration of myelin in the peripheral nerves of the cutis.

Scleredema adultorum may be a unique variety of trophedema.

NOTE.—Since this paper was written Frank [20] has reported a case of scleredema adultorum (Buschke). The patient, a man aged 22, was confined to bed for six days with tonsillitis. A week thereafter he complained of "transitory shooting pains in the back of the neck." Induration of the face, the neck and the tongue followed. It is unfortunate that in the histologic data there was no mention of any myelin sheath staining for the cutaneous nerves. The shooting pains, however, suggest an involvement of the peripheral nerves. Frank found "a sparse perivascular round cell infiltration" but "no changes in the blood vessels themselves." Such a negative finding in relation to structural change in the endothelial cells of the blood vessels does not preclude a disturbance in the function of the blood vessels. An alteration in the tone of the nervous influences supplying the capillaries might have produced a disturbance in permeability without demonstrable structural change.

20. Frank, Louis J.: Scleredema Adultorum (Buschke), Arch. Dermat. & Syph. **36**:1052 (Nov.) 1937.

SYNDROME OF SPOON NAILS, ANEMIA, CHEILITIS AND DYSPHAGIA

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The purpose of this paper is to call attention to the dermatologic features of a syndrome variously designated as dysphagia and anemia, the dysphagia of anemic women, idiopathic hypochromic anemia and achylic chloranemia, but perhaps better known as the Plummer-Vinson syndrome.

My interest in this syndrome was stimulated by the following case:

REPORT OF A CASE

Mrs. A. C., aged 69, was first seen Nov. 24, 1936, complaining of an eruption on the lower lip of eight weeks' duration. This eruption began shortly after the lower lip had become chapped following sunburn. Since the onset the lip had never resumed its normal appearance. Occasionally painful cracks and fissures had occurred, and the lip had repeatedly scaled. One year before admission the patient had had a similar condition of the lip, which lasted three or four weeks but healed rapidly after the use of zinc oxide ointment.

The past history revealed a tendency to recurrent herpes simplex involving the lower lip. For the past forty years the patient had had difficulty in swallowing. She attributed this to a "contracted throat" following diphtheria. Formerly she had been troubled with indigestion, but since she had eaten strained vegetables, for the past twenty years, the indigestion was no longer present. Her diet consisted of from 1½ to 2 quarts (1,420 to 1,890 cc.) of milk daily, a great deal of sugar and candy, considerable coffee, ice cream sodas, small amounts of fruit juices, creamed soups, farina and strained vegetables. Meats and salads were entirely lacking. Further inquiry brought out the fact that her skin had always been sensitive to sunlight. Exposure to the sun for five or ten minutes would cause her to become nervous and shaky.

On examination the pale, bloodless appearance of the skin was striking. The palpebral conjunctiva and the lobes of the ears were pale. There was difficulty in getting sufficient blood from the lobes of the ears to make a blood count. The entire vermilion border of the lower lip was red, and the central part of the lip presented a peculiar scaly, crusted and granular appearance. The finger nails were not examined at this time. The tongue was smooth and glazed, and definite atrophy of the papillae was present.

A blood count showed 35 per cent hemoglobin, 5,190,000 red cells and 4,600 white cells. The results of the differential smear were as follows: 53 per cent

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Read at the Sixtieth Annual Meeting of the American Dermatological Association, Inc., Cresco, Pa., June 4, 1937.

neutrophils, 35 per cent lymphocytes, 4 per cent monocytes, 4 per cent basophils and 4 per cent eosinophils. One nucleated red blood cell was seen; hypochromasia, achromasia and anisocytosis were present.

The patient was given large doses of iron and liver (lextron capsules) by mouth and four small doses of unfiltered roentgen rays to the lower lip at weekly intervals. Six weeks later the lip was apparently normal, and the hemoglobin content had risen to 80 per cent. The patient looked better and stated that she felt a great deal better.

Shortly after the patient's first visit, a case of cheilitis, anemia and spoon nails was reported.[1] The patient's nails were then examined. The toe nails were normal, but the nails of the index and middle fingers presented a definite spoon shape (fig. *A*), and the free edges had a frayed or gnawed appearance (fig. *B*). On May 24, 1937, six months after the patient was first seen, the nails were normal.

The patient thus disclosed the following definite syndrome: dysphagia of forty years' duration, a marked but peculiar type of anemia, spoon nails, an atrophic tongue and cheilitis.

SPOON NAILS

Most of the early writers dealing with the Plummer-Vinson syndrome entirely overlooked the condition of the nails or did not deem the changes of sufficient importance to be included in their reports. In the sixty-nine cases from the Mayo Clinic reported by Vinson [2] in 1922, there was no mention of any changes in the nails. Moersch and Conner [3] reported sixty-five cases from the same clinic four years later, and failed to mention the condition of the nails. In recent years, however, an increasing number of observers in all parts of the world (England,[4] Germany [5] and France [6]) have called attention to the fact that koilonychia often accompanies a definite type of anemia.

This fact should not be interpreted to mean that anemia alone causes spoon nails. We are aware of the familial occurrence of spoon nails, as mentioned by Pardo-Castello.[7] He spoke also of the occurrence of koilonychia with lichen planus, with syphilis as reported by Howard Fox,[8] with acanthosis nigricans, with prolonged cachexia, with monile-

1. Lewis, Beatrice: Cheilitis Associated with Microcytic Hypochromic Anemia, Brit. J. Dermat. **48**:32 (Jan.) 1936.

2. Vinson, Porter P.: Hysterical Dysphagia, Minnesota Med. **5**:107, 1922.

3. Moersch, Herman J., and Conner, H. Milton: Hysterical Dysphagia, Arch. Otolaryng. **4**:112 (Aug.) 1926.

4. Klaber, Robert: Idiopathic Hypochromic Anemia with Dermatitis Herpetiformis, Brit. J. Dermat. **48**:504 (Oct.) 1936.

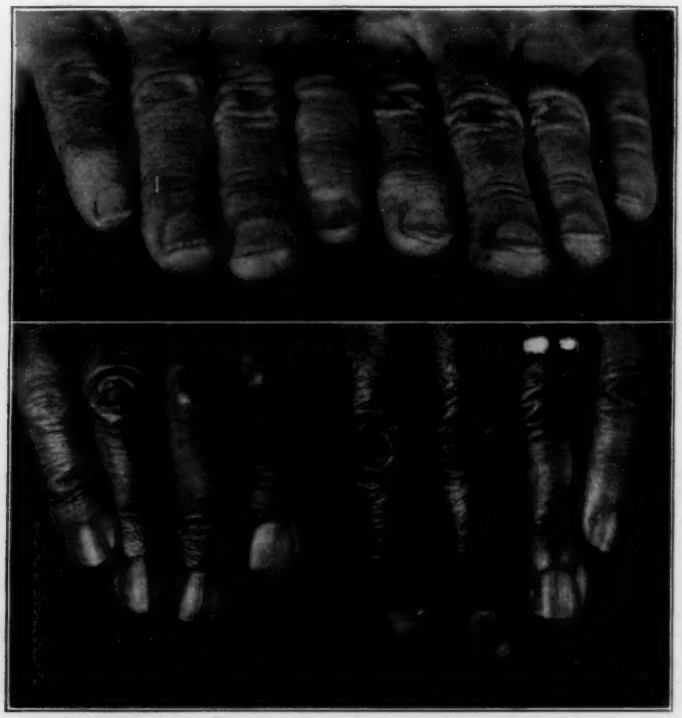
5. Rosegger, H.: Koilonychia (Spoon Nails), Med. Welt **10**:1803 (Dec. 12) 1936; abstracted, J. A. M. A. **108**:515 (Feb. 6) 1937.

6. Weissenbach, R. J.; Martineau, J., and Stewart, W.: Koilonychia, Hypochromic Anemia and Achlorhydria, Bull. Soc. franç. de dermat. et syph. **44**:390 (March) 1937.

7. Pardo-Castello, V.: Diseases of the Nails, Springfield, Ill., Charles C. Thomas, Publisher, 1936.

8. Fox, Howard: Spoon Nails (Koilonychia), Arch. Dermat. & Syph. **2**: 265 (Aug.) 1920.

thrix as reported by Walzer,[9] in certain dystrophic states [10] and possibly as secondary to a fungous infection.[11] It should be noted that external factors may produce spoon nails, notably in persons whose hands are in hot soap suds, alkalis or acids for long periods. Koilonychia has been reported as affecting persons having frequent contact with oils, creosotes and cresols and workers with coal.[5] The most complete account of koilonychia in the English literature is that of Cipollaro.[12]



The upper photograph shows koilonychia of the index and middle fingers; the lower, complete disappearance of koilonychia after six months of iron and liver therapy.

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9. Walzer, Abraham: Monilethrix and Koilonychia, Arch. Dermat. & Syph. **21**:1011 (June) 1933.

10. Wander, W. G.: Dystrophy of the Finger Nails and Toe Nails (Spoon Nails), Arch. Dermat. & Syph. **27**:1011 (June) 1933. Maire and Woringer: A Case of Koilonychia Cured After Pluriglandular Therapy, Bull. Soc. franç. de dermat. et syph. **37**:1214 (Dec.) 1930. A case is reported of a girl aged 9 with dystrophy of the hair and palmar hyperkeratosis. Her basal metabolic rate was —47. Treatment with thyroid extract was followed by marked improvement.

11. Wise, Fred: Spoon Nails (Koilonychia), J. Cutan. Dis. **37**:467 (July) 1919.

12. Cipollaro, Anthony C.: Koilonychia: Report of a Case and a Review of the Literature, New York State J. Med. **30**:380 (April 1) 1930.

In cases in which spoon nails seem to be associated with some or all of the various components of the Plummer-Vinson syndrome, the most constant finding is that of an associated anemia. All the nails may manifest the changes, but in varying degrees. The toe nails are usually normal. The cuplike or spoonlike depression of the nail is centrally located, and may be of such a degree that a drop of water placed in it would remain there. The lunula of the nail is usually intact, and the normal luster may or may not be preserved. There is often a noticeable exaggeration of the fine longitudinal striations, and the nail may be soft, both friable and fragile, with a splitting of the free border. Occasionally transverse elevations or ridges occur. The skin about the nail shows no signs of any eczematous process or other abnormality.

There may occur periods of incomplete improvement in the condition of the nails, alternating with periods of aggravation. Benefit has been reported by Broekema [13] and others by treatment with liver extract and iron. In general, the changes in the nails in koilonychia may be said to be a part of the Plummer-Vinson syndrome. It is difficult to estimate the percentage of cases in which changes in the nails occur, for the earlier observers either were unaware of the changes or regarded them as of little importance. It may be said, however, that with the increasing number of reports of cases in which spoon nails are associated with anemia, a complete blood count should be made in every case of this condition.

ANEMIA

The anemia, which is perhaps the constant and the most striking feature of this syndrome, has been present in every reported case. Women—for this syndrome is practically confined to the female sex—present a definite and peculiar pallor, which at times closely resembles that of pernicious anemia. The changes in the blood in over two hundred cases reported by many different observers are those of mild secondary anemia, but with a marked and constant reduction in the amount of hemoglobin. The red blood cell count in over two hundred cases averaged about 4,000,000, but the hemoglobin content was reduced to approximately 50 per cent.

Because Graham and Johnson [14] have noted an increased fragility of the red blood cells in each of their six cases, they feel that the anemia is a new and peculiar one of a specific type. Apparently the red blood cells of other patients with severe secondary anemia show no such increased fragility.

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13. Broekema, J. H.: Koilonychia and the Stomach, Acta dermat.-venereol. **14**:113 (June) 1933; cited by Pardo-Castello.[7]

14. Graham, G., and Johnson, R. S.: Anemia with Dysphagia, Quart. J. Med. **1**:41 (Jan.) 1932.

Whether the anemia is caused by the dysphagia and consequently is on a nutritional basis or whether the dysphagia follows the anemia is a question on which no agreement has been reached.

Associated with the anemia in a high (75-90) percentage of cases, one finds achlorhydria, and in a lesser proportion (25-30 per cent) there occurs enlargement of the spleen. As in pernicious anemia, there is little, if any, loss of weight.

CHANGES IN THE MUCOUS MEMBRANES

The changes in the mucous membranes which occur in the Plummer-Vinson syndrome are fairly constant and involve the lips, the tongue and buccal mucosa, the pharynx and the upper part of the esophagus. The lips, which are pale, may present varying degrees of inflammation. In some instances the cheilitis is barely perceptible, while in others there may be a marked hypertrophic granular cheilitis. In most cases soreness or fissures are present at one or both corners of the mouth, simulating perlèche.

Most patients are edentulous, the teeth having usually been extracted in an attempt to relieve the dysphagia. The tongue is smooth, glazed, atrophic and devoid of papillae. It is interesting to note that regeneration of the lingual papillae may occur under treatment with iron,[15] although there is some experimental and clinical work to show that the smooth tongue is probably due to a deficiency in the diet or to inability of the patient to absorb vitamin B.[16] The buccal mucosa tends to be dry, pale, lusterless and atrophic.

The pharyngeal mucosa is pale and atrophic and lacks normal resiliency. Fissures easily occur after manipulation. In many of the cases reported by English, and to a lesser extent in those reported by American, observers,[17] there have been definite bands or webs in the upper part of the esophagus. These webs have produced an actual narrowing of the esophageal lumen.

DYSPHAGIA

The dysphagia which is present in many cases begins suddenly, often following a severe nervous or emotional shock. The dysphagia is confined to the level of the larynx, and many patients complain of an unusual tightness of the throat. Some patients complain of thyroid trouble to the physician when they seek relief.[17] Because of the dysphagia solid foods, including meats, fruits and vegetables, are early omitted from

15. Suzman, M. M.: Syndrome of Anemia, Glossitis and Dysphagia, Arch. Int. Med. **51**:1 (Jan.) 1933.

16. Hutter, Adolph M., and Middleton, W. S.: Vitamin B Deficiency and Atrophic Tongue, J. A. M. A. **101**:1305 (Oct. 21) 1933.

17. Hoover, W. B.: The Syndrome of Anemia, Glossitis and Dysphagia, New England J. Med. **213**:394 (Aug. 29) 1935.

the diet. The food has to be masticated slowly and with great care. The diet is markedly reduced, tea, coffee and semisolid foods becoming the daily fare. The patients often prefer to eat alone because of the time required to masticate their food completely. The dysphagia is more marked when the patient is nervous and tired; so it is more troublesome at the evening meal than at breakfast. Periods in which the dysphagia is absent may occur, and at such times patients are able to eat normally. Such periods of remission are of short duration and usually terminate suddenly, with physical or mental fatigue.

It is interesting to note that dysphagia is often completely relieved by mechanical dilation of the esophagus, such as the passage of an esophageal bougie. Hence most American writers have regarded dysphagia as being of a functional or hysterical nature.

RELATION OF THE PLUMMER-VINSON SYNDROME TO CANCER OF THE UPPER PART OF THE ALIMENTARY TRACT

Kelly,[18] Paterson,[19] McGibbon,[20] Cameron [21] and more recently Ahlbom [22] have all called attention to the possibility of malignant disease in the late stages of this syndrome. In six of seven cases reported by McGibbon there were definite organic esophageal lesions, and in the seventh case there were multiple malignant new growths of the buccal mucosa. This condition may be related to the frequent occurrence of esophageal cancer at this site in women.

Ahlbom cites two instances of multiple carcinoma of the lip and oral cavity in women presenting the Plummer-Vinson syndrome. One of these women had five carcinomas of the lip and oral cavity, and the other had three carcinomas. Ahlbom found that either achlorhydric anemia or the Plummer-Vinson syndrome was present in about half of all women with carcinoma of the mouth and in a great majority of women with carcinoma of the hypopharynx or of the upper portion of the esophagus. These instances are more important because of the fact that since 1931 Ahlbom has observed two hundred and fifty women with squamous cell carcinoma of the mouth, pharynx or esophagus. One hundred and fifty of these women were questioned and examined with

18. Kelly, A. Brown: Nervous Affections of the Esophagus, J. Laryng. & Otol. **42**:221, 1927.

19. Paterson, D. R.: Obstruction at the Upper End of the Esophagus, J. Laryng. & Otol. **46**:532, 1931; A Clinical Type of Dysphagia, ibid. **34**:289, 1919.

20. McGibbon, John: The Esophageal Lesions Encountered in Cases of Dysphagia with Anemia, J. Laryng. & Otol. **50**:329, 1935.

21. Cameron, J. A. M.: Dysphagia and Anemia, J. Laryng. & Otol. **44**:168, 1929; Quart. J. Med. **22**:43 (Oct.) 1928.

22. Ahlbom, Hugo E.: Simple Achlorhydric Anemia, Plummer-Vinson Syndrome and Carcinoma of the Mouth, Pharynx and Esophagus in Women, Brit. M. J. **2**:331 (Aug. 15) 1936.

reference to signs and symptoms suggesting achlorhydric anemia or the Plummer-Vinson syndrome, and in about 70 per cent of the women the symptoms were present.

TREATMENT

The treatment of the Plummer-Vinson syndrome consists of relief of the dysphagia by mechanical measures. This is accomplished by the passage of an esophageal sound or dilator, a single treatment often relieving the dysphagia for many months.

The anemia is best treated by means of some iron compound, such as iron and ammonium citrate in a daily dose of 3 Gm. or ferrous carbonate in a daily dose of 5.4 Gm. The use of liver extract alone has proved disappointing, but the simultaneous use of liver extract and iron probably produces the most rapid improvement. With the disappearance of the dysphagia, foods high in iron and vitamin content can be added to the diet.

SUMMARY

A case of the Plummer-Vinson syndrome is presented.

The following various features composing this syndrome have been briefly discussed: spoon nails, anemia, dysphagia and changes in the mucous membranes.

The possible relationship of this syndrome to carcinoma of the upper part of the alimentary tract in women has been briefly mentioned.

ABSTRACT OF DISCUSSION

DR. ROBERT L. GILMAN, Philadelphia: I have been extremely interested in the case Dr. Anderson described, for I know that many dermatologists have had the experience I have had in the last several years, of seeing more and more cases of "sun allergy." The majority of these cases have been characterized, as Dr. Anderson said, by cheilitis or herpes simplex. My experience parallels Dr. Anderson's in that all patients I observed were women past 30 years of age. It seems that after a certain age women tolerate the sun less and less. I wonder whether this intolerance is not due to the many fads in diet and the exposure to the sun that people are indulging in. Dr. Anderson listed carefully the diet of this patient. I recall that symptoms of pseudopellagra developed in a patient who was in the hospital two years ago on a modified diet for relief of ulcer. The condition seemed to be a marked avitaminosis. In the last few years I have used vitamins B and C in treating patients sensitive to the sun and have secured marked improvement. There seems to be considerable benefit with the intake of supplementary vitamin preparations, and improvement is contingent on their use.

DR. NELSON PAUL ANDERSON, Los Angeles: Dr. Weidman wishes me to explain why this patient did not take more orange juice in California. I am sure I do not know. There are several other interesting facts. Plummer and Vinson have called attention to the fact that in cases in which the syndrome has existed for a long time symptoms of mild hypothyroidism often develop when the anemia improves. Hence Plummer and Vinson believe that small doses of thyroid are indicated. It is possible that the changes in the nails may be due not to changes in the blood or to an avitaminosis but to decreased activity of the thyroid gland.

CUTANEOUS MANIFESTATIONS OF TRICHOPHYTON PURPUREUM (BANG)

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ROYAL M. MONTGOMERY, M.D.

AND

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It is sometimes possible to recognize that an infection of the skin is caused by a particular pathogenic fungus from the characteristic cutaneous manifestations. Thus, it is well known that the bilateral, superficial, circumscribed, erythematous and scaly eruption of the upper part of the inner aspect of the thigh is commonly caused by Epidermophyton cruris. One may often suspect that an infection of the scalp is caused by Microsporon lanosum from the history of contact with an infected animal, the short duration, the tendency to spontaneous cure and the inflammatory character of the lesions. Infections of the scalp caused by Microsporon audouini, Trichophyton violaceum, Microsporon fulvum and Achorion schoenleinii may exhibit clinical characteristics which lead one to suspect the identity of the fungus causing the infection. Infections of the skin due to Monilia albicans and the lesions of blastomycosis, actinomycosis and sporotrichosis have clinical expressions characteristic of the infecting organism. From a study of lesions of the skin and the nails of one hundred patients from whom we recovered Trichophyton purpureum, it is our belief that such lesions are so characteristic that one may usually recognize the identity of the infecting micro-organism from clinical inspection alone.

REVIEW OF THE LITERATURE

We have been able to find only a few definite references to the cutaneous manifestations of T. purpureum (Bang). According to Djélaleddin-Moukhtar's [1] report in 1892 of the clinical types of ringworm

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The material in this paper formed the basis for an exhibit in the Scientific Section at the Eighty-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 7 to 11, 1937.

1. Djélaleddin-Moukhtar: De la trichophytie des régions palmaire et plantaire, Ann. de dermat. et. syph. **3**:885, 1892.

of the hand and of the foot, the conditions in some of his cases resembled the infections described in this paper. In Bang's [2] original description of T. purpureum he said it was recovered from an erythematous, scaly eruption on the smooth skin of the arms and the abdomen. Castellani [3] a little before Bang reported on a new species which he called Epidermophyton rubrum. This organism was recovered in a case of tinea cruris. In Hodges' [4] cases of onychomycosis, Trichophyton "A" and Trichophyton "B" (which are similar, if not identical, to T. purpureum) were frequently found in the infected nails. Priestley [5] in Australia isolated Trichophyton rubidum from the erythematosquamous eruption of a soldier. This organism is probably the same as T. purpureum or a species related to it. In case 1 reported by Hartzell [6] the clinical characteristics and the course pointed to an infection with T. purpureum. Cultures of the causative fungus were not obtained. Ota [7] in 1922 mentioned the frequent occurrence in Japan and in Manchuria of eruptions due to this organism. He said that

> it is the chief cause of eczema marginatum, at times of herpes circiné and dyshidrotic ringworm, and rarely of onychomycosis. In Japan and Manchuria, eczema marginatum is rarely caused by Epidermophyton inguinale (Sabouraud) compared to those caused by this species of trichophyton.

The supposed rarity of involvement of the nails by T. purpureum in Japan is surprising, and the impression may be open to revision. Kittredge [8] reported a case of extensive fungous infection of the glabrous skin simulating tinea imbricata and associated with onychomycosis universalis. The causative organism had characteristics similar to those of T. purpureum and was probably this fungus or one closely related to it. In a later report Kittredge [9] described a second case of universal

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2. Bang, H.: Sur une trichophytie cutanée àgrands cercles, causée par un dermatophyte nouveau (Trichophyton purpureum Bang), Ann. de dermat. et syph. **1**:225 (May) 1910.

3. Castellani, A.: Observation on a New Species of Epidermophyton Found in Tinea Cruris, Brit. J. Dermat. **22**:147 (May) 1910.

4. Hodges, R. S.: Ringworm of the Nails, Arch. Dermat. & Syph. **4**:1 (July) 1921.

5. Priestley, H.: Ringworm and Allied Parasitic Skin Diseases in Australia, M. J. Australia **2**:471 (Dec. 8) 1917.

6. Hartzell, M. B.: Two Unusual Cases of Ringworm, One of Them Due to a Fungus (Trichophyton Rosaceum) Producing Pink Cultures, Arch. Dermat. & Syph. **1**:1 (Jan.) 1920.

7. Ota, M.: Contribution to the Study of Trichophyton Purpureum Bang, Trichophyton Interdigitale Priestley and Trichophyton "B" Hodges, Arch. Dermat. & Syph. **5**:693 (June) 1922.

8. Kittredge, H. E.: Trichophytosis, Including Onychomycosis Universalis, Simulating Tinea Imbricata, Arch. Dermat. & Syph. **27**:607 (April) 1933.

9. Kittredge, H. E.: Onychomycosis Universalis Trichophytina et Epidermophyta, Arch. Dermat. & Syph. **34**:398 (Sept.) 1936.

infection of the nails and found that in this case, the seventh on record, the causative organism was likewise T. purpureum. Two cases each were reported by Kato [10] and by Takeya,[11] and in all of these T. purpureum was isolated from patients with tinea capitis. Dodge [12] expressed doubt that the organism isolated by Kato [10] was T. purpureum and stated the opinion that the fungus might be "a red member of the Favotrichophyton violaceum group." Harris and Lewis [13] in 1930 reported the case of a man with bandlike granulomas on the neck. T. purpureum was cultured from hairs from the site.

Payenneville and Rivalier [14] studied a patient who had an extensive and bizarre, erythematous, scaling eruption, from which they repeatedly isolated T. purpureum. They stated that this organism is rarely seen in France; in this instance the source of the infection was Anam. Cure followed the topical use of 1 per cent tincture of iodine.

Geographic Distribution.—According to Weidman,[15] T. purpureum is not uncommon in Manchuria, Japan or the southern part of the United States. The organism is found in almost all parts of the world but has been considered the cause of cutaneous diseases in only a small percentage of the reported cases of fungous infection. It is our belief, since the organism is being isolated more frequently now than formerly, that this fungus is responsible for an increasing number of infections of the skin in New York. This is in line with the opinion of Weidman,[16] who stated that "the prevailing species in a given country tends to vary over periods of years." In a report by Kittredge [17] on ringworm of the nails, in twenty out of thirty-five cases which he collected from the literature T. purpureum or a related organism was found.

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10. Kato, Y.: On the Ringworm of the Scalp Caused by Sabouraudites Ruber (Epidermophyton rubrum Cast.) Especially on Its Character of Endothrix, Jap. J. Dermat. & Urol. **25**:895, 1925.

11. Takeya, M.: Trichophytia Capillitii Caused by Trichophyton Purpureum, Jap. J. Dermat. & Urol. **26**:7, 1926.

12. Dodge, C. W.: Medical Mycology, St. Louis, C. V. Mosby Company, 1935, p. 488.

13. Harris, J. H., and Lewis, G. M.: Trichophyton Purpureum (Bang) as a Deep Invader of the Skin, Arch. Dermat. & Syph. **22**:1 (July) 1930.

14. Payenneville, J., and Rivalier, E.: Un cas d'épidermophytie exotique, Ann. de dermat. et syph. **8**:378 (May) 1937.

15. Weidman, F. D.: Laboratory Aspects of Epidermophytosis, Arch. Dermat. & Syph. **15**:415 (April) 1927.

16. Weidman, F. D.: Infections, in Blumer, George: The Practitioners Library of Medicine and Surgery, New York, D. Appleton-Century Company, Inc., 1936, vol. 10, p. 118.

17. Kittredge, H. E.: Ringworm of the Nails, Urol. & Cutan. Rev. **38**:875 (Dec.) 1934.

Nature of the Organism.—From a comparison of our findings with the published studies of Bang,[2] Castellani,[3] Priestley,[5] Ota,[7] Carrión [18] and others, it would seem that the organisms described by these authors are probably related if not identical. Hashimoto, Irizawa and Ota [19] expressed the belief that many of the reported species were identical. Muskatblit,[20] however, described differences in cultural characteristics and in types of spores between T. purpureum (Bang) and E. rubrum (Castellani). Dodge [21] described Epidermophyton purpureum (T. purpureum [Bang]), Epidermophyton rubidum (T. rubidum [Priestley]) and E. rubrum (Castellani) as distinct species. Bruhns and Alexander [22] in Jadassohn's *Handbuch* listed the following as synonymous: E. rubrum (Castellani), T. purpureum (Bang), T. "A" and T. "B" (Hodges), T. purpureum (Ota), T. rubidum (Priestley) and Sabouraudites rubra (Ota and Langeron [23]). Weidman [24] has remarked on the tendency of T. purpureum to exhibit variants. We have noted that in many of our strains individual peculiarities developed. In their essential characteristics, however, a certain uniformity among the growths was noted. Since the clinical picture appears to be one that rarely deviates from the pattern described in this paper, additional evidence is offered that the strains responsible for the disease in our cases must be closely related.

THE PRESENT STUDY

In the following brief discussion a description is given of the organism which we isolated from the lesions of one hundred patients. We have not felt justified in inoculating this organism into human subjects, since such infections offer considerable resistance to treatment. We have not had the opportunity to perform experiments with animals.

Selection of Material.—It may be opportune to note that T. purpureum is sometimes difficult to isolate, unless care is used in selecting

18. Carrión, A. L.: Preliminary Report on the Fungus Causing Epidermophytosis of the General Surface of the Skin in Porto Rico, Porto Rico J. Pub. Health & Trop. Med. **5**:40 (Sept.) 1929.

19. Hashimoto, T.; Irizawa, T., and Ota, M.: Une variété blanche du Sabourauditis ruber (Epidermophyton rubrum ou purpureum), Jap. J. Dermat. & Urol. **30**:243 (March) 1930.

20. Muskatblit, E.: Observations on Epidermophyton rubrum or Trichophyton purpureum, Mycologia **25**:109 (March-April) 1933.

21. Dodge,[12] pp. 485-488.

22. Bruhns, C., and Alexander, A.: Allgemeine Mykologie, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, p. 221.

23. Ota, M., and Langeron, M.: Nouvelle classification des dermatophytes, Ann. de parasitol. **1**:305 (Oct.) 1923.

24. Weidman, cited by Kittredge.[9]

suitable material for examination. We have found that this fungus invades nail tissue deeply. For this reason, the superficial part of the nail should be scraped or clipped away and discarded. In several instances we have demonstrated Trichophyton gypseum from the top layers of the nail and T. purpureum from the lower portions. The incidence of contaminants, such as Aspergillus and Hormodendron, diminishes as the top part of the nail is removed. Numerous scrapings from suspected cutaneous lesions may be necessary before T. purpureum can be demonstrated.

Microscopic Appearance of Fungus in Scrapings.—There is nothing characteristic here. While the amount of fungous material may be

Fig. 1.—Appearance of T. purpureum on dextrose agar after two weeks.

sparse, we have occasionally noted large numbers of organisms in a specimen. The mycelium is of approximately the same size as that of T. gypseum (about 3 or 4 microns in diameter).

Cultural Characteristics.—On dextrose agar, in primary growth, the culture at first is fluffy, pure white and hemispherical. The edge of the colony becomes less fluffy and at times is granular. The under surface of the colony shows a typical rose-purple color, which gradually spreads to the edge of the colony and may be noted in varying degrees throughout the colony. Pleomorphism occurs eventually.

Appearance of Cultures under Filtered Ultraviolet Rays: The colors are bright but hazy. The central half of the colony is mauve; the remainder is a light soft blue violet.

Culture Mount: There are many sterile vegetative hyphae and many microconidia in thyrses and in grapelike clusters. Fuseaux are few. Chlamydospores develop in older growths.

Inoculation of Animals.—Inoculation of animals is occasionally successful. Bang,[2] Ota[7] and Hodges[4] reported positive results in the inoculation of guinea pigs. Castellani[3] was unsuccessful in similar attempts.

Index of Sensitization.—The index of sensitization is low. It is similar to that of A. schoenleinii and/or of T. violaceum, in that patients infected with the organism reveal a negative or only slightly positive reaction to trichophytin.

Clinical Manifestations.—In an analysis of the lesions in the skin and the nails of one hundred patients from whom we were able to recover T. purpureum certain features occurred with sufficient regularity to make it unnecessary to repeat the details of each individual case. There were sixty-three male and thirty-seven female subjects. The duration of the infection varied from two weeks to seventeen years; the average was three years. There was little tendency to spontaneous remission or cure, although the lesions on the skin frequently became more troublesome (pruritic) and more active during the summer. The majority of the patients were born in the United States; many had never been abroad. The infection appears to have been contracted in New York in a large percentage of this group. In approximately 40 per cent the birthplace was a foreign country, the following countries being represented: Russia, Italy, Austria, Hungary, Germany, Poland, Finland, Albania, Portugal, Mexico, Puerto Rico and China. While the source of the infection is purely speculative in some instances, it is certain in other instances that the infection originated in some of those countries. It would thus appear that a fairly representative series of specimens, geographically and racially speaking, was obtained for mycologic study. The incidence according to the region of the body is shown in the table. A summary of the chief features of the findings in different sites follows:

Location of Infection Caused by T. Purpureum in One Hundred Patients

	Skin	Nails	Skin and Nails	Follicles	Total Infections
Feet	72	40	26	..	86
Hands	20	28	9	..	39
Trunk, arms and legs	15	..	..	..	15
Inguinal region	12	..	..	..	12
Trunk (gyrate)	4	..	..	..	4
Face	1	..	..	1	2

1. Hands and Feet: The appearance of the eruption due to T. purpureum on the feet and on the hands appears to be peculiar to this organism. Lesions of the feet may occur on the soles, the sides, the dorsa, the toes and the nails. The plantar surface is a common site. When the hands are involved, the palms, the dorsa, the fingers or the nails may be affected. Itching is frequent.

The entire sole is frequently involved, but the infection may be localized to a small area around the heel or on the ball of the foot. When the sole is involved, the infection usually extends to the sides of the foot and about the heel. The infected skin is dull red and slightly thickened or indurated. The scaling, which is constant, is usually fine and thin (branny), in comparison to the large flaky scale found in psoriasis or in some types of dermatophytosis. The absence of visible vesiculation in the infected area is a persistent feature. There is usually a sharply marginated border along the outside of the foot between the infected skin and the normal skin on the dorsum of the foot.

Fig. 2.—Dull red scaly eruption extending on the side of the foot.

Small, irregular, infiltrated, erythematous and scaly patches may be found on the dorsum of the foot and the toes. The degree of erythema may vary within a single patch. There is no tendency to central clearing.

The infection of the under surface of the toes and of the interdigital webs is clinically similar to the infection of the sole, with the addition of a certain amount of maceration. When the entire area about the toe is infected, the skin appears thickened and dry. Painful fissuring may occur about the joints.

The eruption on the hands is similar to that on the feet. The entire palm may exhibit the characteristic dull red color, with thickening and scaling. Friction and frequent washing in all probability make the scaling less apparent than that on the soles. The erythema may be slight and the condition thus be considered a callus. Isolated irregular patches may be present about the dorsum of the hand and the fingers, as is the case on the feet. Frequently the skin of an entire finger is

involved. Redness of the skin over the joints of the hands with or without scaling may be noted. Fissuring in affected patches about the joints is a fairly constant feature. The absence of vesiculation and itching is again notable. On several occasions when the palm was involved we observed a marked decrease in the amount of sweat.

2. Nails: Nails infected with any pathogenic fungus except M. albicans are opaque, lusterless, friable and yellowish. Varying degrees of dystrophy, as evidenced by irregularities of the nail plate, separation of the nail and subungual hyperkeratosis, are frequently present.

Nails infected with T. purpureum sometimes have certain features peculiar to this organism and not entirely shared by nails infected by other fungi. Unlike infections of the nails caused by T. gypseum, there is not a frequent concomitant involvement of the interdigital webs of the toes. Furthermore, a superficial location of the infection on the surface of the nail is frequent with T. gypseum but practically unknown with T. purpureum. The duration of the infection is shorter, and the progress of the infection is faster with T. gypseum than with T. purpureum.

The onset and progress of the ungual infection due to T. purpureum is slow and insidious. When the condition is first observed, one or more nails may be involved. Frequently toenails and even the feet may be found to be infected without the knowledge of the patient, who has applied for treatment of infected fingernails. There is little reaction in the subungual and paronychial tissues. We have not observed paronychia in any of our cases.

The infection usually begins under the free border or along the lateral margins of the nail plate. We have observed one case in which the infection started in the proximal portion of the nail. Yellow or white vertical streaks may appear in the nail and seem to be the result of separation of the nail plate from its bed. These streaks gradually widen; the nail separates more and more, and débris accumulates. There may be a gradual involvement of the distal end of the nail, without the usual formation of streaks. Meanwhile, the nail itself becomes thinned, owing to gradual invasion of the fungus. The nail becomes brittle and may be broken or worn off in its distal portion, leaving only the proximal part. Sometimes the entire nail plate is lost, leaving the nail bed covered with scales and accumulated débris.

In no case have we been able to isolate T. purpureum from the surface of nails either obviously infected by fungi or showing no evidence of fungous involvement. In connection with this observation, we should like to point out that scrapings from the surface of infected nails frequently contained the ordinary saprophytes, but when scrapings from the deeper portions of the nail were planted on agar slants, T. pur-

pureum in pure culture resulted. For this reason cultures of infected nails should be taken from different depths in the nail substance. Unless the deeper portions are examined, and even when they are, a number of scrapings may be required before the organism can be cultured.

The presence of an infected fingernail should always invite examination for infected toenails, since the two sites are frequently simultaneously affected. The following case is briefly reported to illustrate the nature of the involvement of the skin and the nails on the hands and the feet:

REPORT OF CASE

CASE 1.—S. K., a man aged 31, a teacher, had an eruption on the hands and the feet for over fifteen years. He first noticed the eruption soon after working in his father's fur shop. It started on the index finger of the left hand; within a year several fingernails were infected, and within three years scaling and redness appeared on the hands, the wrists and the feet.

The patient's father had a similar eruption of the hands, the feet and the toenails, and T. purpureum was cultured from the lesions.

Examination showed thickened and scaly patches on the palms and the fingers and some fissuring at the joints. The erythematous areas extended across the dorsa of the hands and the knuckles. There was no visible vesiculation. The nails of the left hand were yellowish, friable and opaque, with considerable destruction of the distal portions. Several nails were dystrophic. The nails of the right hand showed separation from the nail bed and subungual hyperkeratosis. There was no paronychia. On the feet a small amount of interdigital maceration and some fissuring were noted. The soles were infiltrated, scaly and dull red. Patches similar to those on the hands were present about the heels and on the dorsa of the feet. All the toenails were affected in the same manner as the fingernails. This would appear to be the eighth instance of universal fungous infection of the nails to be reported.

The patient had had varied treatment previously, including roentgen and ultraviolet irradiation, injection of a bismuth preparation, oral administration of arsenic and potassium iodide and surgical removal of several of the nails. The various external applications used had included potassium permanganate, ammoniated mercury, chrysarobin and salicylic acid. He had a long course of injections of trichophytin and is now using concentrated compound ointment of benzoic acid, which has produced some improvement.

After repeated examinations fungi were found in scales from a finger and since their first appearance have been found repeatedly on the nails, the fingers and the soles. The organism has always been T. purpureum. The Wassermann reaction was negative, and a specimen of urine showed no abnormality. The reaction to trichophytin was weak. The histologic picture of a section removed from a patch on the foot showed a simple inflammatory process.

3. Glabrous Skin: Infections on the smooth skin may be divided into several types. There is rarely any noticeable vesiculation. Lesions have been observed to spread to the hairy parts, such as an eyebrow or the back of the neck, without involving the hair follicles. We have found classification according to type of lesion convenient, thus:

In type A the lesions are circinate. Dull red scaly areas develop. These show a tendency to ring formation, clear in the center and have a superficial resemblance to tinea circinata.

Solid plaques characterize type B. Such lesions are not unlike certain lesions of psoriasis, being dull red and scaly on the surface, with slight thickening. Bleeding points are usually not present when the scales are removed. The intensity of the color may vary in different portions of a single patch. The shape of the lesions may not necessarily be regular. The size of the patches varies from that of a pinhead

Fig. 3 (case 1).—Superficial scaling and thickened callus-like areas on the hand.

to that of a half dollar or larger. There is no tendency to central clearing. Lesions have been noted on various portions of the trunk, on the extremities and in one instance on the face.

In type C the lesions are bizarre and configurate. We have observed three instances of eruptions involving large surfaces of the skin of the trunk. The infection begins at one or more points and migrates in a thin line in an ever-widening area. The affected skin shows the same general characteristics of dull red color, slight infiltration and scaling

on the surface as in type B. Behind the advancing border the skin is of a lighter color than normal. This suggests partial achromia. Persistent itching is a constant feature, and excoriations are usually seen.

The lesions in type D resemble those in tinea imbricata. We have not observed any case similar to that reported by Kittredge,[8] in which the disease simulated tinea imbricata. In his case the lesions first suggested ichthyosis; itching was marked, and the process went on for a long period.

In the following case configurate and bizarre lesions (type C) were present on the trunk, and there was involvement of the left hand and of the feet:

CASE 2.—F. C., a man aged 25, a laborer, gave a history of contact with horses for ten years. Five years previously lesions had appeared on the feet; for three years the shoulder had been involved, and for one and one-half years the chest and the left hand had been affected.

Fig. 4.—Destruction of the nail plate and undermining are characteristic features of infection with T. purpureum.

On the upper portion of the chest, the left shoulder and the back were large circinate plaques (fig. 7). The border of the lesions was raised, well defined and irregular. It appeared to be made up of pinhead-sized erythematous papules, some of which were covered with a yellowish scale. There was apparent depigmentation in the central portion of the plaques on the chest and the back. This area was scaly. There were several erythematous, scaly, papular lesions on the dorsum of the left hand and the fingers. Circinate lesions extended about the wrist. The left palm was thickened and slightly scaly. Both soles were erythematous, thickened and scaly. There were irregular, scaly patches on the dorsum of the foot. The nails were not infected.

Fungi were present on the feet, the back, the hands and the chest. Cultures from the hands and the feet showed T. purpureum. The Wassermann reaction was negative. Urinalysis showed no abnormality. The trichophytin test gave negative results. A biopsy specimen taken from the back showed a simple inflammatory process in the upper part of the cutis.

An ointment containing 6 per cent each of salicylic acid and ammoniated mercury resulted in the eventual cure of the lesions on the body. The lesions on the hands and the feet have proved more resistant and are still present.

4. Groin: The infection in this location may be unilateral or bilateral and is frequently associated with involvement of the intergluteal fold, of the scrotum, of the pubis or of other adjacent areas of skin. The affected skin assumes the same characteristics noted in type B on the glabrous skin. Pruritus is frequently a distressing symptom.

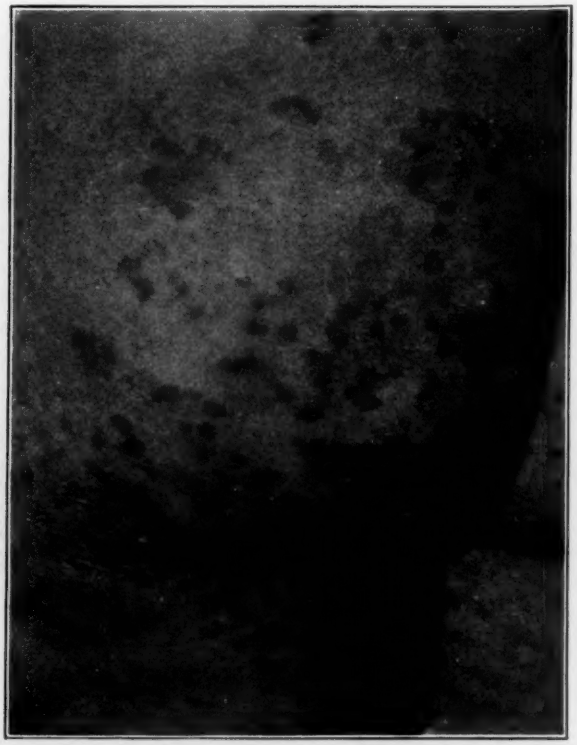

Fig. 5.—Dull red, scaly, superficial lesions present for three years and resistant to treatment.

5. Hair Follicles: Follicular infections due to T. purpureum are rare, and only five previous reports [25] of infection of the hair follicles have been found. In a sixth case which we have observed the infection was of further interest because it was on the upper lip, a rare location for a fungous infection.

Case 3.—I. F., a man aged 62, consulted us because of cutaneous lesions on his hands and feet of three years' duration. Other areas of the skin became

25. Kato.[10] Takeya.[11] Harris and Lewis.[13]

involved during the preceding few months. Examination showed that all the nails of the toes were involved and were yellowish, opaque and crumbly; toward the base some of the nails were thickened, and in the great toenails, subungual hyperkeratosis was present. The nails of the right hand were involved and had a similar dystrophic appearance, being yellowish and friable and in certain instances showing vertical grooves. There was superficial scaling on the palmar surfaces and on the sides of the fingers. Erythematous and scaly areas were noted on the dorsum of the right hand. On the plantar surfaces were thickened and scaly dull red patches. On the buttocks were several superficial, scaly dull red patches, and there were similar sharply marginated plaques on the inner aspects of both thighs.

The upper lip was the site of scattered follicular papules and superficial pustules (fig. 8). A few similar lesions were scattered through the remainder of the beard.

Fig. 6.—Well defined, dull red, scaly, pruritic plaque, simulating psoriasis or neurodermatitis.

Examination showed fungi on the right hand, the right fingernails, the soles, the toenails, the groin, the buttocks, the beard and the upper lip. Cultural studies of material from all these sites revealed T. purpureum. Hairs in the follicular lesions of the upper lip and the beard, examined in filtered ultraviolet light, showed dull gray fluorescence. There was some confusion, however, in interpreting the nature of this fluorescent effect, since gray hairs in other areas of the beard showed a similar fluorescence. The Wassermann reaction was negative. Cutaneous tests with trichophytin revealed a mildly positive reaction at the test site.

Examination of the infected hairs from the upper lip showed no actual invasion of the hair shaft. The fungous elements were present only on the surface of the hair or in the débris attached to the hair. This would appear to substantiate the view of Harris and Lewis [13] that T. purpureum is an ectothrix.

Trichophytin Tests.—The immune reactions in patients with fungous infections caused by T. purpureum are similar to those noted in

patients with favus and in patients with infections caused by T. violaceum. The usual finding is either a negative or a weak reaction at the site of the intracutaneous injection of the test dose of trichophytin.

Histologic Picture.—There would appear to be marked uniformity in the pathologic changes in infections caused by T. purpureum. This uniformity finds expression in a nonspecific inflammatory process. We have not observed any deviation from this picture in the numerous specimens we have studied. A summary of the histologic findings by Dr. Wilbert Sachs follows:

A simple inflammatory process is present in the upper part of the cutis and is of mild degree. The vessels are slightly dilated; cellular elements are of the small round type and are sparse. There is moderate interstitial edema. The epidermis is slightly acanthotic. The basal cell margin is intact. There is no intercellular edema, spongiosis or vesicle formation; occasionally areas of parakeratosis are noted. In two specimens there are single minute cavities, similar to

Fig. 7.—Large gyrate areas showing apparent achromia. Smaller scaly lesions may be noted within the advancing border.

those noted in so-called pustular psoriasis. In the latter condition, however, the cavities are much larger. In one specimen the picture is not incompatible with early pyogenic folliculitis. This specimen was removed from a gyrate patch on the trunk. No organisms were seen in any of the sections. The pathologic diagnosis is a superficial simple inflammatory process.

Differential Diagnosis.—In all instances the demonstration of the organism in culture is the final proof. The histologic picture of a mild inflammation may be helpful in a negative way.

1. Hands and Feet: Psoriasis, arsenical keratosis, calluses, eczema and neurodermatitis may be suspected. The absence of concomitant lesions, the atypical nature of the lesion when closely examined and the absence of bleeding points when the scale is removed may assist in ruling out psoriasis. Arsenical keratoses show more localization on the palms and soles, and punctate hyperkeratosis is present. There is no

sharp margin on the sides of the feet or the hands. On the palms and the soles we have noted several examples of callus-like tinea caused by T. purpureum. The absence of a history of manual labor or of friction, the presence of a dull red reaction in the lesions and the superficial scaling will serve to differentiate the condition from callus. The dry form of eczema and of neurodermatitis show more acute inflammation and more tendency to involve the backs of the hands. The lichenification of neurodermatitis is characteristic. The dull red color, the indolent nature of the lesions, the slight branny scaling and the presence of concomitant lesions in suggestive locations should be sufficient to afford a basis for a tentative diagnosis of fungous infection due to T. purpureum.

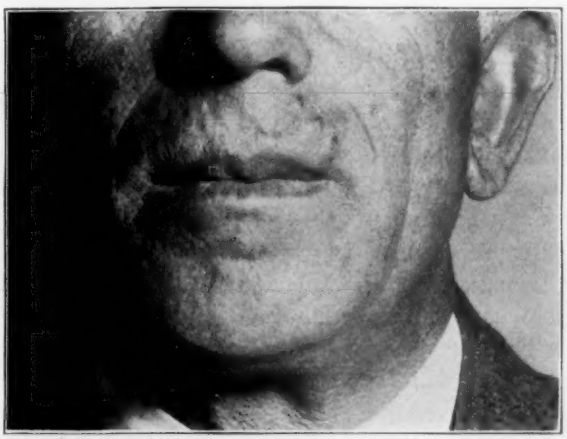

Fig. 8 (case 3).—Involvement of the upper lip, the sixth reported instance of follicular infection in man due to T. purpureum.

2. Nails: T. purpureum may be suspected as the infecting cause in onychomycosis because of the long duration, the slow course, the presence of vertical streaks in the nail substance and the deep position in the nail of the fungous elements. In infections by T. gypseum the duration is short, the involvement is fast, the superficial part of the nail may become involved and concomitant interdigital involvement is common. The chief characteristics of fungous infection (such as crumbling, opacity and yellow color) rule against psoriasis. In psoriasis the nail is usually hard. Puncta are frequently present. Other areas of infection may be present. If the organism is not found after repeated examinations, ungual dystrophy from some other cause is likely.

3. Glabrous Skin: Psoriasis in atypical forms, neurodermatitis in unusual locations and erythema annulare centrifugum (Darier) may

be simulated. In psoriasis the scales are flaky and silvery, and on their removal bleeding points may usually be observed. The scales in lesions due to T. purpureum are fine, and when they are removed bleeding points are not usually produced. The absence of concomitant lesions on the scalp or on the extensor surfaces of the arms and the legs should make one suspicious of an infection due to T. purpureum. The histologic picture may be of particular importance here. Neurodermatitis exhibits lichenification; it is probably more pruritic than tinea due to T. purpureum, and there are no concomitant lesions elsewhere to suggest other forms of infection. The presence of scales on the surface of the lesions, the intense itching, the absence of edematous plaques and the lack of temporary remissions may serve to direct suspicion toward an infection caused by T. purpureum rather than toward erythema annulare centrifugum (Darier).

4. Groin: Tinea cruris when caused by T. purpureum may be unilateral or bilateral; the infection frequently spreads to the intergluteal fold and to the scrotum. When Epidermophyton cruris is the causative fungus, the infection is nearly always bilateral and seldom spreads to adjoining areas of skin. Pruritus is more intense in infections due to T. purpureum.

5. Follicular Infection: In the one case of involvement of the beard which we studied it was impossible to differentiate the condition clinically from sycosis vulgaris. When traction by forceps was employed, the hairs were epilated more readily and the operation caused less pain than when hairs present in follicles which are the sites of pyogenic sycosis are removed. This may be a distinguishing feature between the two conditions.

Treatment.—We have attempted cure by means of injections of several different commercial extracts of fungi (trichophytin) without success. The use of roentgen or ultraviolet rays has not proved effective in our hands. The internal administration of potassium iodide has likewise been of no therapeutic value. In all forms of the infection the persistent use of strong antiparasitic remedies over long periods has given the best results. Chrysarobin (mentioned in Bang's original article [2]), anthrarobin and compound ointment of benzoic acid N. F. have proved their value. At times such remedies have to be temporarily abandoned and soothing remedies applied. Nails should be mechanically scraped before each application of the medicament, since the organism grows best in the deeper portion of the nail substance.

SUMMARY AND CONCLUSIONS

In one hundred cases of fungous infection involving various parts of the body T. purpureum was isolated.

The clinical characteristics of the regional manifestations are given. There is rarely any deviation from the usual picture.

Infections caused by this organism may be more numerous in New York than formerly.

The various clinical manifestations may simulate psoriasis, arsenical keratosis, neurodermatitis, eczema, sycosis vulgaris and erythema annulare centrifugum (Darier). At times the diagnosis may be made with certainty only from cultural studies.

An instance of follicular infection and one of infection of all the nails of the hands and the feet, both of which are rare, are recorded.

The reaction to trichophytin in patients with infections due to T. purpureum is either negative or slightly positive.

The histologic picture consistently is that of a simple inflammatory process.

The infections caused by this fungus are difficult to cure. At present chief reliance must be placed on strong topical remedies used for a considerable length of time.

200 West Fifty-Ninth Street.

57 West Fifty-Seventh Street.

301 East Nineteenth Street.

Clinical Notes

TREATMENT OF A PEMPHIGOID ERUPTION WITH SULFANILAMIDE

Report of a Case

EVERETT S. LAIN, M.D., AND JOHN H. LAMB, M.D., OKLAHOMA CITY

Since the advent of sulfanilamide, its administration has been tried in the treatment of many diseases which have been more or less resistant to other methods. Results in cases of erysipelas have been striking in our hands, as they have been in other cases in which infectious lesions were suspected to be of streptococcic origin.

Welsh[1] was able to isolate from the nasopharynx of patients with pemphigus streptococci which were virulent for five species of animals and was able to produce lesions consistent with pemphigus in a fair number. Since he was able to produce pemphigoid bullae by intradermal and subcutaneous injections of these dead streptococci in patients with pemphigus, we decided to try this new drug in the first case of pemphigus we observed in which no previous treatment had been given.

REPORT OF CASE

On Jan. 30, 1938, a farmer aged 48 was referred to us. He had noticed a reddish eruption on his back two months previously, which later became moist, although at the time he was not certain about blisters. The next lesions appeared around the scalp and four weeks ago began to spread over the entire body. He had applied zinc oxide only to the lesions and stated that he had not taken any medicine by mouth. The lesions, however, became progressively worse, and large blisters began to appear. The patient stated that when he was in the army a diagnosis of "soldier's heart" had been made. He alleged that he had had a fast heart ever since childhood, after an attack of scarlet fever. He complained of no shortness of breath, no swelling of the ankles and no fainting spells. He had recently noticed that he became exhausted easily and did not feel normal in any respect. His appetite was slightly subnormal, but he had not lost much weight. Examination of the blood showed 95 per cent hemoglobin, 5,040,000 red cells and 4,100 white cells. The Wassermann reaction was negative.

Examination.—The eruption was distributed from head to foot but was worse around the axillae, the elbows, the back, the neck and the inner aspects of the thighs. It consisted of small to medium-sized vesicles and bullae containing seropurulent material. Some of the bullae were as large as 3 or 4 cm. in diameter. The oral mucosa was markedly congested, and there were some early lesions in the mouth. There were a few lesions scattered over the face, the scalp and the feet. Several lesions on the abdomen were circinate and after complete rupture of the bullae left raw, tender, marginated bases. Examination of the heart showed no murmurs but only a rapid pulse.

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1. Welsh, A. L.: Specificity of a Streptococcus Isolated from Patients with Pemphigus, Arch. Dermat. & Syph. **30**:611 (Nov.) 1930.

Treatment.—On February 1 the patient was given 30 grains (1.94 Gm.) of sulfanilamide in divided doses; on February 2 he was given 40 grains (2.59 Gm.), and 45 grains (2.92 Gm.) was then given daily until February 7, when the dose was reduced to three tablets, or 15 grains (0.97 Gm.), daily. Fading of the eruption was noticed within thirty hours and then became almost spectacular. After three days nearly all the old lesions were exfoliating, and only one or two small new ones had appeared on the chest. On the sixth day no new lesions had appeared, but there had appeared on the posterior parts of the thighs and the buttocks an eruption which was red and only slightly vesicular. We suspected that this secondary eruption might have been caused by the sulfanilamide. The dose was then reduced to 15 grains (0.97 Gm.) daily, after which no new lesions of any character formed and the secondary eruption on the buttocks and the thighs disappeared.

Pemphigoid eruption before treatment with sulfanilamide.

On February 11 a notation was made in the record that all lesions had completely subsided and exfoliated. By February 14 no bullae had appeared, but there had appeared on the face and the hands an erythematopapular eruption similar to the previous secondary eruption on the buttocks and the thighs. Administration of sulfanilamide was discontinued, and the eruption rapidly subsided. The patient's skin has remained clear for four weeks at the time of this report. He is taking only one 5 grain (0.32 Gm.) tablet of sulfanilamide every other day.

COMMENT

It is probable that sulfanilamide is being used in the treatment of pemphigoid eruptions in many clinics and by individual dermatologists and that this will prove or disprove its value in the treatment of this disease. We have used it in a few cases of dermatitis herpetiformis. One patient who has had the disease for many years reports that at the time of this writing he is approximately free from all lesions as a result of this medication. We have not, however, seen such a spectacular recovery from an eruption resembling pemphigus through the use of any

other medicinal agent. After our patient had apparently recovered, Caro [2] reported two cases in which pemphigus had been cleared by the use of this drug after previous treatment had failed. We admit that not enough time has elapsed to allow us to evaluate the possibility of recurrences in cases of pemphigus, but we trust that a new weapon has been added to the equipment for the treatment of this disease.

SUMMARY

Spectacular cure of a pemphigoid eruption by the use of sulfanilamide is reported.

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2. Caro, M. R.: Pemphigus: Treatment with Sulfanilamide, Arch. Dermat. & Syph. **37**:196 (Feb.) 1938.

Obituaries

RAYMOND SABOURAUD, M.D.

MYCOLOGIST, BACTERIOLOGIST AND DERMATOLOGIST

1864-1938

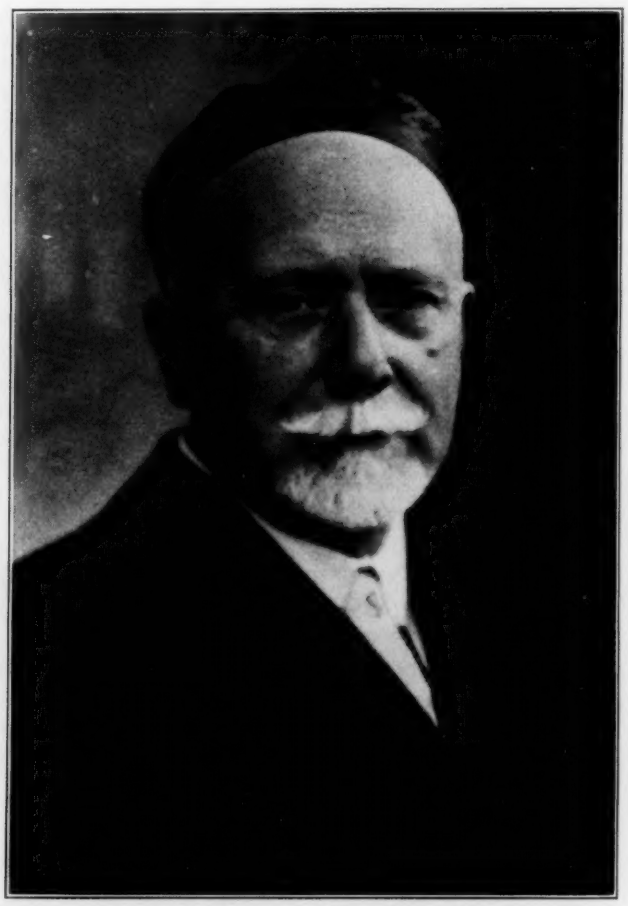
Sabouraud died Feb. 4, 1938, at the age of 74. With his passing not only the French school of dermatologists but dermatologists in every country of the world suffered a severe loss. Here in the United States, where Sabouraud's revolutionary treatise on the microsporon was to be confirmed for the first time outside France, in 1899, by members of the New York Dermatological Society, and where live so many of his former pupils, his passing is especially felt. Sabouraud was an honorary member of every national dermatologic society in the world, for his classic works on ringworm, impetigo, seborrhea, eczema and the group of diseases known as the pityriases were recognized as masterpieces based solely on personal scientific investigations lasting over forty years.

His publications are too well known and too numerous to be mentioned here. If collected they would comprise twenty large volumes. When it is considered that not one of his articles revamped the work of some previous writer insight into the character of Sabouraud is immediately attained.

His genius was based on two main characteristics, which were his throughout life: originality of thought and belief and a superlative tenacity of purpose. Early in his career he planned to write five volumes on the disease of the hair and its follicle. The first three volumes, the last of which covered the tineas, were published between 1902 and 1910. An interval of eighteen years of research and clinical observation passed before he felt capable of publishing the fourth volume, dealing with eczema and pyodermic infections. Sabouraud was 64 years old at that time. The next year volume 5, entitled "La pelade," appeared. Sabouraud often said that eczema and alopecia areata were the two most difficult subjects he had studied, for so much that was false and contradictory had been written about both over fifty years. Who would believe today that Unna, one of the world's greatest dermatologists, would have thought that seborrheic eczema was due to a dyshidrosis, i. e., an excessive function of the sweat glands? Who would think today that any doubt could exist as to the organism causing impetigo contagiosa? It was Sabouraud who proved that seborrhea and

not sweat was the prime factor in seborrheic eczema and the acnes and established beyond a doubt that impetigo contagiosa is caused by a streptococcus and that the staphylococcus is a secondary invader that outgrows the streptococcus in twenty-four hours.

The apex of his personal investigations was reached when he published his book on ringworm, in 1910. In his studies on ringworm



RAYMOND SABOURAUD, M.D.
1864-1938

Sabouraud started from scratch, as nothing definite was known about the subject in the last two decades of the nineteenth century. David Gruby's works, published from 1842 to 1847, were either disbelieved or entirely forgotten. As a matter of fact, ringworm of the scalp and alopecia areata were hopelessly confused by all dermatologists of this

period, although the existence of fungous infections of the scalp was admitted by all.

Sabouraud had four years' internship in the service of Ernest Besnier and of A. J. L. Brocq just after his graduation from medical school. Two of these years were spent in the histologic laboratory of the Saint-Louis Hospital. He had a year of bacteriology at the Pasteur Institute under the renowned teachers Emile Roux and Elie Metchnikoff. He was fitted to study the clinical as well as the mycologic side of ringworm. He was able to establish for the first time the individuality of the different species of cryptogamic parasites and to connect the clinical picture of the disease with the exact causative agent. Probably his greatest contributions were the finding of a medium on which the fungi always reproduced themselves with a constant exactitude and the description of a proper technic for studying these organisms. All this knowledge was based on twenty years of original work, and he carefully preserved until his retirement preparations by which every one of his results could be verified.

From a practical point of view, the most important part of his studies on ringworm was the perfection, in collaboration with his associates Noiré and Pignot, of a method of epilation of the hair by the use of roentgen rays. This method, now used over the entire world, has reduced the duration of treatment from two years to two months. In 1900 he was appointed head of the École Lailler, a combined school and hospital having a capacity of 300 beds. In four years, thanks to his new method of treatment, he turned back 150 beds to the Saint-Louis Hospital. Pautrier figured that these beds represented a capital saving of 1,500,000 francs per year at that time, which is roughly equivalent to 10,000,000 francs today. This method of treatment has prevented epidemics and reduced the number of cases of ringworm in France to such an extent that the École Lailler today has only 20 beds. Sabouraud loved to teach, and his lectures were made available to students and practitioners in his three informal volumes entitled "Dermatological Conversations," which were published at various times. In 1932 his studies of the diseases of the scalp were summarized in a practical form under the title of "Diagnosis and Treatment of Diseases of the Scalp." An earlier work called "A Manual of Regional Topographical Dermatology" was written in six weeks on a bet, to confute some of his critics who accused him of being only a laboratory worker.

Sabouraud had an engaging personality. His laboratory during the last twenty years that he was director of the École Lailler was the goal for all students of mycology and trichology. He was equally kind and courteous to the visiting neophyte and the visiting professor. Transfer colonies of his collection of ringworm cultures could be had for the asking.

So much for Sabouraud the scientist, who is well known to every one. The life of Sabouraud outside of medicine is really a surprise and a revelation. His antecedents for generations were either physicians or artists. Before his marriage, in his late thirties, Sabouraud spent his leisure moments on Saturday afternoons and Sundays in the art museums of France or in searching for rare forms of mushrooms with his faithful laboratory assistant, Paul. His enthusiasm for the arts finally culminated in his becoming a sculptor of high renown, and his talent along this line was recognized throughout France when a book reproducing his statues was published a few years ago.

In addition, he found time to cultivate rare species of plants and flowers at his summer home on the Marne, in the vicinity of Paris, France. His happy family life with his wife and three children was a proof that science and domesticity can go hand in hand.

In the last decade of his life, which was saddened by the tragic death of his wife, his son and his beloved son-in-law in rapid succession, he began to write philosophic essays, which were as full of wisdom and originality of thought as were his medical books. The most recent of these books, entitled "Sur les pas de Montaigne," appeared just before his death.

Sabouraud took to his bed a week before his death and died peacefully. He retained his full intellect to the end and was thankful that his Creator had allowed him such a full and useful life.

Dermatologists in the United States join with those in France in grieving for Sabouraud, the man who not only brought glory to the French school of dermatology but may be considered as one of the truly great savants of the time.

LEE MCCARTHY, Washington, D. C.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

SOLITARY CUTANEOUS AND SUBCUTANEOUS LEIOMYOMA. ARTHUR PURDY STOUT, Am. J. Cancer **29**:435 (March) 1937.

The author reports 15 cases of solitary leiomyoma, 4 of cutaneous and 11 of subcutaneous involvement. He expresses the opinion that the condition is probably as common as multiple leiomyoma. These tumors are usually benign, of long duration and of small size and frequently are characterized by paroxysmal pain. They are distributed on the extensor surfaces of the upper and lower extremities, the scrotum, the labium majus, the nipple or its areola or the cheeks. They occur in two morphologic types, one consisting of neoplastic smooth muscle fibers and a peculiar venous structure and the other simply of smooth muscle tissue. The former apparently arises from the smooth muscle of the involved vein and the latter usually from one of the arrector pilorum muscles. Glomus tumor and fibrosarcoma must be differentiated.

MULTIPLE GLOMIC TUMORS. HILDING BERGSTRAND, Am. J. Cancer **29**:470 (March) 1937.

Glomic tumors are usually small, single, tender or painful deep cutaneous tumors, possibly identical with angiosarcoma and perithelioma. The writer reports 2 cases, in each of which the lesion was situated subcutaneously on the foot. Histologically, the tumor tissue consisted of a tangle of peculiarly constructed, thick-walled vessels, the walls of which consisted solely of large epithelium-like cells in a stroma of fine collagenous filaments, or a mixture of such cells and smooth muscle cells. Large numbers of nerves were observed between the vascular structures.

FOERSTER, Milwaukee.

RECURRENCE IN MIXED TUMORS OF THE SOFT PALATE. JONATHAN E. RHOADS and PAUL M. MECRAY, Am. J. M. Sc. **193**:389 (March) 1937.

Although mixed tumors of the soft palate resemble those of the parotid gland, recurrence after excision is rare. The authors report an instance of recurrence of such a tumor at the original site eleven years after its removal. Only 2 similar recurrences have been described among 60 cases of mixed tumor of the soft palate recorded in the literature.

THE USE OF ACETYL-β-METHYLCHOLINE CHLORIDE BY IONTOPHORESIS IN PERIPHERAL VASCULAR DISEASES. DAVID W. KRAMER, Am. J. M. Sc. **193**:405 (March) 1937.

Thirty patients with peripheral vascular disease were given mecholyl by iontophoresis, and improvement followed in 22 cases. Good results were observed most frequently (87 per cent) in patients with vasospastic involvement; 65 per cent of the diabetic subjects and 55 per cent of patients with Buerger's disease responded favorably. The effect on pain was less noticeable than that on fatigue and on spasm.

The increased and improved peripheral circulatory function observed by the authors was undoubtedly due to the vasodilator properties of this drug.

URINARY EXCRETION OF ARSENIC: I. NORMAL SUBJECTS; II. THE INFLUENCE OF THIOSULPHATE. MARJORIE R. MATTICE and DONALD WEISMAN, Am. J. M. Sc. **193**:413 and 420 (March) 1937.

The authors attempted to determine the daily urinary excretion of arsenic in apparently normal subjects. Their results emphasize the necessity for standardized

chemical procedures, known diet and accurate collection of specimens from patients whose excretion of arsenic is being studied. On an average diet Mattice and Weisman found wide daily variations: from 0 to 0.85 mg. of arsenic, with the mean at 0.26 mg. In only 18 per cent of the 163 subjects did they fail to demonstrate excretion of arsenic in the urine.

The effect of intravenous administration of sodium thiosulfate on the urinary excretion of arsenic was studied with 4 patients on a controlled diet. The authors concluded that under such conditions the urinary elimination of arsenic is diminished not only on the day of administration of the thiosulfate but on subsequent days.

LYNCH, St. Paul.

RESEARCH NEEDS IN THE CONTROL OF SYPHILIS. A. M. CHESNEY, Am. J. Syph., Gonor. & Ven. Dis. **21**:121 (March) 1937.

The author discusses some of the gaps in the present knowledge of syphilis and attempts to point out fertile fields for investigation. Regarding etiology, the inability to cultivate virulent forms of Spirochaeta pallida constitutes the principle obstacle in the path leading to a complete knowledge concerning the etiologic agent of syphilis. Unanswered, too, is the question of why the spirochetes prefer to localize in certain organs or tissues and habitually leave others alone. Why the nervous system is not involved in every case is especially obscure. The close relation between syphilis and trauma would seem to indicate that an investigation along these lines might throw light on the problem of localization. Further unsolved problems are: the nature of the serologic reaction in syphilis and its relation to immunity; knowledge of the defensive mechanism which the syphilitic patient brings to bear on his infection, which knowledge might furnish the means of stimulating that mechanism and even of producing by artificial methods an immunity against that infection, and the problem of the patient with latent syphilis as a carrier. Regarding treatment, it is pointed out that practitioners are still in the dark as to the essential antisyphilitic mechanism of many of the agents in use. According to Chesney, one of the most pressing of all needs in research is that for discovering better drugs that will at the same time bring down the present high cost of, and time required for, treatment.

OPTIMAL TREATMENT FOR EARLY SYPHILIS BASED ON A TWENTY-YEAR TRIAL OF ARSPHENAMINE, BISMUTH, AND MERCURY PREPARATION. A. BENSON CANNON, Am. J. Syph., Gonor. & Ven. Dis. **21**:155 (March) 1937.

The author analyzes the records in 600 cases observed during his twenty years' experience in the treatment of early syphilis. Since 1916 he has followed a plan of continuous treatment, consisting of a total of three courses of ten injections each of an arsphenamine and three courses of fifteen injections each of a mercury or bismuth preparation throughout the first year. Of a total of 236 patients admitted with primary or early secondary syphilis, satisfactory end results were achieved in 92.2 per cent with arsphenamine, in 83.1 per cent with neoarsphenamine and in 82.9 per cent with silver arsphenamine. According to the author, old arsphenamine leads both neoarsphenamine and silver arsphenamine measured by practically every criterion applied, whereas the relative merits of bismuth and mercury preparations are more equally apportioned. The optimum for the average patient with early syphilis is one year of regular and continuous treatment such as the author outlines. The patient's chance of cure decreases directly as the duration of the infection increases, in spite of optimal treatment.

REUTER, Milwaukee.

PSORIASIS. H. ORR, Canad. M. A. J. **36**:165 (Feb.) 1937.

In the treatment of psoriasis Orr separates the patients into two groups. The patients in the first group are in the stage in which new lesions develop; the older lesions are enlarging and Köbner's sign is present. Conservative treatment by soothing topical applications, oral administration of wine of antimony and auto-

hemotherapy is indicated. In the second group of patients no new lesions are forming; there is no extension of older lesions, and Köbner's sign is not elicited. For such patients Orr advises a wide variety of remedies, including stimulating and oxidizing topical remedies and a diet low in protein, fat and calories. Although there are many half-breeds and Indians in Alberta, Orr has never seen psoriasis among them.

THE USE OF MAPHARSEN IN THE TREATMENT OF SYPHILIS. S. C. PETERSON, Canad. M. A. J. **36**:172 (Feb.) 1937.

Peterson used mapharsen for four months in the treatment of patients with syphilis in the Manitoba Government Clinic at the St. Boniface Hospital in Winnipeg. From the effects of 1,814 injections given to 99 patients Peterson was impressed with its performance and expresses the belief that it represents a distinct refinement in arsenical therapy. He found that there were fewer reactions to it and that spirochetes disappeared from surface lesions faster (in 1 instance in twenty-four hours) than with neoarsphenamine.

CLINICAL PROBLEMS IN SYPHILIS CONTROL TODAY. JOHN H. STOKES, J. A. M. A. **108**:780 (March 6) 1937.

Stokes outlines several clinical problems of importance in the control of syphilis. It is essential that the chief of a clinic for the treatment of syphilis be able, vital and interested; he must assume responsibility for all the work in the clinic. Stokes compares the various methods of treatment of early syphilis and stresses the importance of continuous as against intermittent treatment. He points out the danger of lapse of treatment, the importance of the early use of arsphenamine and the fact that the evidence is now in favor of the use of bismuth rather than mercury. The importance of regular serologic testing, the individualization of treatment according to the patient and the technic of obtaining satisfactory data on the spinal fluid are all stressed as important features in the control of early syphilis. The problem of latency is one calling for judgment. Patients in whom latent syphilis is present require a complete physical examination and cautious and intelligent treatment. The syphilitic woman constitutes an additional menace at the onset of pregnancy. Stokes advises two tests of the blood, the first at the third month, which allows for adequate therapy during pregnancy, and the second at the eighth month. Regarding the syphilitic child, Stokes urges the use of intensive arsenical and bismuth therapy for the treatment of interstitial keratitis. Fever therapy is useful in the treatment of prenatal syphilis. Neurosyphilis should be prevented by adequate early treatment; administration of tryparsamide and fever therapy in cases in which treatment has been neglected during the early months have produced good results. Final evaluation of the various methods for producing fever has not yet taken place. Stokes adds several practical hints to prevent trouble: first, to watch for reactions; second, to instruct the patient regarding diet, elimination, etc., and third, to watch for any sign of abnormality, such as itching, fever, pain or changes in the urine or stools. Technical precautions should include looking at the label before injection of medicine, unhurried treatment, inspection of the patient before injection and routine questioning, which may preclude severe reactions.

THE SERODIAGNOSIS OF SYPHILIS. H. H. HAZEN, J. A. M. A. **108**:785 (March 6) 1937.

Hazen reports on the evaluation of the various serodiagnostic tests for syphilis. In an analysis of the results from the standpoint of specificity the following tests were found to be satisfactory: the Brem, the Eagle flocculation, the Kahn (diagnostic and presumptive), the Kline (diagnostic and exclusion), the Kolmer and the Lufkin and Rytz. From the standpoint of sensitivity the leading tests are the Kahn diagnostic and the Ruediger, with the Brem and the Kline diagnostic close

behind. It was interesting to note that 59 per cent of all tests performed on lepers yielded positive results; patients with malaria showed about 15 per cent positive results; tuberculosis, jaundice, malignant growths, acute febrile conditions, pregnancy and menstruation did not affect the results. Hazen is of the opinion that flocculation tests will probably displace the complement fixation tests for the diagnosis of syphilis. The chief points in favor of the former are the relative cheapness, the rapidity and the ease of performance and the fact that only a few drops of blood are necessary.

VISIBLE CONTACT TESTER. AARON BROWN, J. A. M. A. **108**:802 (March 6) 1937.

Brown describes a celluloid apparatus consisting of a spoon and a shield for the application of substances for contact tests. The advantages described are that the reaction, if any, may be observed without removing the application; that aeration is provided, and that the apparatus can be used for liquid as well as for solid substances.

DERMATOLOGIC VERSUS SURGICAL TREATMENT OF CARBUNCLES AND FURUNCLES. SAMUEL AYRES JR., NELSON PAUL ANDERSON and PAUL D. FOSTER, J. A. M. A. **108**:858 (March 13) 1937.

As a result of a questionnaire mailed to 250 surgeons and to the same number of dermatologists, together with the experiences of the authors, an attempt was made to evaluate the methods in use for the treatment of carbuncles and furuncles. It was found that most surgeons employed surgical procedures, such as crucial incision and excision by cautery, in the treatment of carbuncles. The great majority of dermatologists employed conservative methods, such as roentgen and vaccine therapy, injection of bacteriophage and wet dressings. Ayres, Anderson and Foster state that the duration of treatment by a surgical procedure is almost twice as great as that necessary when a more conservative method is used. An additional advantage in conservative treatment is the better final cosmetic result.

LEWIS, New York.

ANAPHYLACTIC SENSITIZATION WITH CHEMICALLY DEFINITE COMPOUNDS. H. E. FIERZ, W. JADASSOHN and W. STOLL, J. Exper. Med. **65**:339 (March) 1937.

It has been known for some time that sensitization can often be produced by protein-free drugs, and this cutaneous hypersensitiveness may become manifest by an urticarial reaction, a type of reaction usually regarded as anaphylactic.

After experimental studies with 5 guinea pigs the authors reached the following conclusions: Chemically definite compounds (drugs) can sensitize animals in the same way that they sensitize human beings. In this process coupling of the chemically definite compound with the protein in the body takes place, and the coupled product sensitizes. The hypersensitiveness caused in this manner cannot be demonstrated with the chemically definite compound used in the preliminary treatment but only with the corresponding azoprotein, which will produce an anaphylactic reaction. The proof of the formation of this azoprotein in vivo, however, makes it likely that chemically definite compounds not only can produce anaphylactic hypersensitiveness but in conjunction with the body protein can induce in the organism an anaphylactic reaction.

CHANGES IN THE CUTANEOUS LYMPHATICS OF HUMAN BEINGS AND IN THE LYMPH FLOW UNDER NORMAL AND PATHOLOGICAL CONDITIONS. PHILIP D. MCMASTER, J. Exper. Med. **65**:347 (March) 1937.

Vital dyes injected intradermally enter lymphatic capillaries directly, render them visible and appear later in the draining lymphatic trunks as colored streamers, thus enabling one to perceive the state of the lymphatic channels and the rate of the flow of lymph within them. Consistent results follow such injection under physiologic conditions known to increase or decrease the flow of lymph.

In the horizontally placed normal limb at rest the flow is slight. In a normal leg or arm hanging downward the flow ceases, although fluid in the limb increases. When a previously dependent arm is raised above the head or when the foot of a seated subject is propped on a table, the flow in the raised limb becomes active. It ceases in the skin of an arm which has been subjected to partial obstruction of the veins by pressure from without, but an active flow of lymph appears during the reactive hyperemia which follows the release of venous obstruction.

LYNCH, St. Paul.

A NEW CASE OF BESNIER-BOECK-SCHAUMANN DISEASE LOCALIZED TO THE EXTREMITIES, WITH AN ABNORMAL ABUNDANCE OF GIANT CELLS IN THE LYMPH NODES AND WITH REMNANTS OF PULMONARY TUBERCULOSIS DISCOVERED BY RADIOSCOPY. L. M. PAUTRIER and P. LANZENBERG, Bull. Soc. franç. de dermat. et syph. **44**:225 (March) 1937.

The case which Pautrier and Lanzenberg discussed was of particular interest because the lesions were limited to the extremities and spared the face entirely, and were of much more rapid evolution than is usual. After three years there was a tendency toward spontaneous regression, without any therapy having been employed.

The lesions in the lymph nodes (epitrochlear group) were characterized by an abundance of giant cells, in addition to the usual histologic features.

Roentgen examination showed that the osseous system was intact but that there were indications of an old tuberculous infection in the lungs. The intradermal tuberculin test gave positive results. Examination of the blood showed polynucleosis rather than monocytosis.

The patient was a man aged 26, who stated there had been no tuberculosis in the family.

The authors commented that Besnier-Boeck-Schaumann disease can occur only after the evolution and cicatrization of the lesions of pulmonary tuberculosis. This does not agree with Schaumann's view that the disease is instigated not by classic tuberculosis but by "benign lymphogranuloma," which, however, has a tuberculous origin and is probably due to bovine bacilli. The coincidental association of pulmonary tuberculosis and Besnier-Boeck-Schaumann disease must be considered. The positive tuberculin reaction in the patient in question and in other patients observed previously suggests that the notion of anergy to tuberculin in Besnier-Boeck-Schaumann disease should be revised.

FETAL ICHTHYOSIS IN A DOG. A. HENRY and LOUIS BORY, Bull. Soc. franç. de dermat. et syph. **44**:325 (Feb.) 1937.

The authors state that the more human and animal dermatoses are compared the more likenesses are noted. They report the case of a pup 7 months old with fetal ichthyosis. The skin was thickened, scaly and without hair over the affected parts. The eruption, which was of linear distribution, involved the front feet and progressed up the sides of the chest. Until the age of 6 months the general health of the animal remained normal. Shortly thereafter the dog had a convulsion, atony of the sphincters and excessive salivation. A similar though shorter crisis occurred five days later.

The authors discuss true and congenital ichthyosis in human beings. True ichthyosis appearing after birth has never been observed in animals. The severe type of fetal ichthyosis (with lesions present at birth) has been noted in animals, almost exclusively in calves. This type of dystrophy, just as in the human being, is incompatible with life.

The benign type of fetal ichthyosis corresponds to Brocq's congenital ichthyosiform erythroderma, and the authors classify the condition in the case in question in that category.

ETIOPATHOGENESIS OF THE SYNDROME OF DE AMICIS. RENATO DE BLASIO, Bull. Soc. franç. de dermat. et syph. **44**:446 (March) 1937.

In 1932 de Amicis, of Naples, Italy, described a particular form of prurigo occurring in Americans visiting in Italy. The disease is manifest by its simultaneous occurrence in several members of the same family. It begins on the patient's arrival and usually but not always occurs in American-born Italians arriving in Italy for the first time.

The eruption is pruritic, made up of small rose-colored papules covered by a bloody crust and located on the trunk and the extremities.

De Blasio concludes that this prurigo-like cutaneous response develops in certain patients when they cross the ocean, as a result of meteorologic and climatic variations.

LAYMON, Minneapolis.

ADSORPTION OF THE VIRUS OF LYMPHOGRANULOMA VENEREUM. A. MIDANA, Gior. ital. di dermat. e sif. **78**:57 (Feb.) 1937.

Midana tried to prove the true physicochemical nature of the virus of lymphogranuloma venereum by observation of the phenomena of adsorption in the presence of animal charcoal, barium sulfate, kaolin and iron oxide. The virus is not adsorbed by animal charcoal, is partially adsorbed by barium sulfate and by iron oxide and is totally adsorbed by kaolin. Midana found that the powders in question show an increase in protein equivalent to the loss of antigenic properties of the virus investigated and therefore concluded that the virus of lymphogranuloma venereum is of the nature of a protein.

PARDO-CASTELLO, Havana, Cuba.

PEMPHIGUS WITH EPIDERMAL CYSTS AND ALBOPAPULOID FORMATIONS. H. CERRUTI and J. DA FONSECA BICUDO JR., Arch. de dermat. e syph. de São Paulo **1**:9 (March) 1937.

The authors report the case of a boy of 16 years with typical dystrophic epidermolysis bullosa hereditaria. A maternal aunt and uncle are said to have similar but less marked conditions; the parents are not consanguineous. The eruption began several years after birth and at the time of examination involved chiefly the feet, the knees, the hands, the elbows and, to a lesser extent, the trunk. There were serous and hemorrhagic bullae, cicatrized atrophic areas, myriads of tiny white grainlike epidermic cysts and dystrophic changes in the nails. Over the lower part of the back the skin was wrinkled like crepe paper and atrophic, giving the impression of papular elevations (albopapuloid formations). The Nikolsky sign was not present except in the atrophic areas. The histologic studies showed edema of the epidermis and the dermis, intra-epidermal and dermo-epidermal bullae, areas of atrophy and epidermal cysts, which at times involved the sweat ducts and the pilosebaceous follicles. A consistent decrease to absence of elastic fibers was evident under the orcein stain in the upper layers of the corium; their amount was normal in the deeper layers. Extensive laboratory studies were made, including tests for hematoporphyrinuria, but no abnormality was discovered. It is noteworthy that while the patient was under observation rheumatic fever developed, with evidences of mitral stenosis and pericardial effusion.

LEIFER, New York.

DRY GANGRENE OF THE FOOT IN A NEWBORN INFANT. N. L. BLOISE, Arch. de pediat. d. Uruguay **7**:467 (Oct.) 1936.

A 2,600 Gm. full term infant on the third day after a normal birth presented cyanosis, coldness and absence of arterial pulsation in one foot. The condition became progressively worse, until dry gangrene of the toes ensued. Three weeks later there was spontaneous amputation of the phalanges, with subsequent recovery up to three years later. During the illness the infant had a trace of albumin in

the urine; the sugar content of the blood was normal, and the Wassermann reaction was negative. The mother, however, was syphilitic, with positive serologic reactions, and had received only irregular treatment during her pregnancy. For this reason Bloise attributes the gangrenous process to vascular changes of syphilitic origin.

SCHLUTZ, Chicago. [AM. J. DIS. CHILD.]

CONTRIBUTION TO THE KNOWLEDGE OF MORBUS BOURNEVILLE-PRINGLE AND OF RECKLINGHAUSEN'S NEUROFIBROMATOSIS. W. L. L. CAROL and J. C. VAN HEUSDEN, Arch. f. Dermat. u. Syph. **175**:1, 1937.

Two cases of typical adenoma sebaceum (Pringle) are reported with tuberous sclerosis, associated with soft fibroma (molluscum pendulum). This association has suggested a connection between adenoma sebaceum and Recklinghausen's disease. Six cases of adenoma sebaceum accompanied with tuberous sclerosis (in 4 of which soft fibroma was not present) and 6 cases of Recklinghausen's neurofibromatosis were studied for comparison. In adenoma sebaceum the soft tumors were longer and narrower than in Recklinghausen's disease and were located on the nape of the neck, the axillae, the loins, the scrotum and the shoulder blades. In Recklinghausen's disease there was irregular distribution over the entire body, especially on the back and the chest, fewer tumors being on the face and the extremities. The fibromas were soft and did not give the sensation of hernia present with Recklinghausen's disease. Examination of 223 soft tumors showed only fibrous tissue and no nervous elements. Other examinations showed no sign of either disease in the same patient. The authors conclude that adenoma sebaceum and Recklinghausen's disease are separate entities.

BECKER, Chicago.

RATE OF GROWTH OF THE SCALP-HAIR. H. TANINO, Hihu-to-Hitunyo **4**:546 (Oct.) 1936.

Among the Japanese apparently only the Buddhist orders (monks and nuns) consistently shave the scalp closely enough to render measurements of the cut-off sections of hair a reliable criterion of the rate of its growth, and this is done only in the region of the vertex capitis. Consequently, the author measured under the microscope the removed stubs of hair, from consecutive tonsures when practicable, of 46 monks from 16 to 49 years of age and 87 nuns from 15 to 56 years of age, at intervals varying from less than four to more than nine days and estimated the rate of growth for each day by averaging the lengths of large numbers (fifty) of hairs from each shaving. Although the inadequacy of material for sweeping conclusions is appreciated, the author expressed the belief that the following conclusions are tentatively justified: 1. The daily rate of growth of the scalp hair of these Japanese religionists is approximately 0.5 mm. 2. The rate of growth of the scalp hair of the men begins to decrease after the twentieth year; with women the rate increases up to the thirtieth year and then suddenly begins to diminish. 3. With each added day's growth between tonsures there seems to be an evident falling off in the rate of growth.

CALCIFIED EPITHELIOMA. K. YOSIKAWA, Hihu-to-Hitunyo **5**:10 (Feb.) 1937.

The paper consists of a brief statistical study of the 28 cases of calcified epithelioma already reported in the Japanese medical literature and a report of the author's own 2 cases. Of these, in case 1 there was a solitary hard mass beneath the skin of the temporal region, and in case 2 there were three hard masses on the outer aspect of the upper part of the right arm. All showed the typical regularly arranged epithelium-like cell nests, surrounded by a dense connective tissue capsule.

Although an indication of continuity between the capsules of some of the sebaceous and sweat glands and melanin-like pigment in the cells of the cell nests in the second case suggest the possibility that the tumor originated in these

glands, especially the pigmented basal cell layer of the epithelium, nevertheless the presence of tiny cell nests similar to the main ones and the lack in places of any definite capsule preclude in the author's mind the possibility of origin in the cutaneous adnexa. The author expresses the belief that there is sufficient evidence (the uniformity in size and shape of cells, their regularity and arrangement, the absence of metastases, etc.) to justify the theory that these tumors originated as an inwandering of embryonic epithelial buds, either during the fetal period or after birth.

THE SO-CALLED SCHIZOSACCHAROMYCOSIS OF BENEDEK. T. ARAKAWA, Hihu-to-Hitunyo **5**:36 (Feb.) 1937.

An eruption most nearly resembling erythrasma covered in patches almost the entire body of a woman of 27 years and that of a young man of 22 years. From the scales of recent lesions of both patients and from the blood of the second was cultured on 8 per cent dextrose agar (according to the directions of Benedek) a large rodlike bacillus, multiplying by fission and splitting sugars in such a manner as to cause its recognition as the organism described by Benedek in 1926 and subsequently. Agglutination reactions in both cases and the intracutaneous reaction in the second case were positive. That the cultured material was toxic to animals was demonstrated rather convincingly by intracutaneous injection into a rabbit and by intraperitoneal injection into a mouse. Human inoculation gave indefinite results.

Four intracutaneous injections of an autogenous vaccine resulted in great improvement in the young man's condition in about one month, the patient seeming at this time to be well on the way to cure. The first patient did not return for treatment.

The author does not attempt to discuss the matter of classifying his organism, other than to identify the disease tentatively with schizosaccharomycosis hominis of Benedek; nor does he attempt to establish it as the causal organism in any independent cutaneous disease.

BRENNAN, Chicago.

CONTRIBUTION TO THE KNOWLEDGE OF ADENOMA SEBACEUM (BASED ON STUDIES OF CEREBROSPINAL FLUID ENCEPHALOGRAMS, ETC.). YOSHIO HIRAGA, Jap. J. Dermat. & Urol. **41**:63 (Feb.) 1937.

The author has studied the encephalogram and the cerebrospinal fluid of 4 patients with adenoma sebaceum, 2 of whom suffered from epileptiform attacks and 1 showed impaired intelligence. Three patients who showed a slightly increased pressure of the spinal fluid had abnormal encephalograms, there being dilatation of both ventricles in 1 and of only the right lateral ventricle in the others. The absence of shadows in the inferior horns of the lateral ventricles, noticed in one case bilaterally and in another case on the left, was the result of fluid in the ventricles. The cause of the dilatation of the ventricles in adenoma sebaceum is probably tuberous sclerosis of the brain. The author could not find any definite connection between the mental and nervous symptoms and the changes in the brain, for 1 patient who showed nervous symptoms had a normal encephalogram, while the patient without any mental or nervous symptoms had an abnormal encephalogram. The author expresses the belief that the manifestation of tuberous sclerosis by clinical symptoms or by the encephalogram depends on the extent and the location of the involved area.

HISTOLOGIC STUDIES OF HUMAN SKIN: IV. ON THE NATURE OF SENILE CHANGES OF THE SKIN. I. EJIRI, Jap. J. Dermat. & Urol. **41**:64 (Feb.) 1937.

The author has studied the elastic and the collagenous tissue in the skin of adults, in order to determine the nature of their changes with advancing age. He made the following observations: The elastic fibers may form shoals with increasing age. The elastic and collagenous fibers undergo changes with age,

the latter disappearing after gradual atrophy while the former become coarse, show granular disintegration and finally undergo vitreous changes. The changed collagenous fibers show generally weaker reactions to staining than the normal ones, while the elastic fibers show peculiar reactions to staining by different methods. The author did not find any transitional state between elastic and collagenous tissue, although he compared many slides stained by numerous methods. The author easily proved that the substance in the upper layer of the cutis which shows peculiar changes with increasing age consists of changed elastic fibers and not of collagenous fibers. In the pathogenesis of senile changes of the skin, the topographic anatomic condition and the effect of cold are probably important factors.

BLOOM, New York.

Society Transactions

BRONX DERMATOLOGICAL SOCIETY

THEODORE ROSENTHAL, M.D., *President*

Nov. 22, 1937

HENRY SILVER, M.D., *Secretary*

Asymptomatic Syphilis Associated with a Positive Wassermann and a Negative Laughlen Test. Presented by DR. LOUIS CHARGIN.

P. G., a Negro aged 52, states that in 1918 he had a sore on the penis. He never received antisyphilitic treatment. Physical examination showed no abnormality. Examination of the blood on two occasions showed a 4 plus Wassermann reaction. The Laughlen test gave negative results on both occasions.

DISCUSSION

DR. LOUIS CHARGIN: The purpose of presenting this patient is to point out the variance in results between the Wassermann test and the newly described precipitation test of Laughlen. My associates, Dr. Churg and Dr. Sobel, and I have been engaged recently in the study of this test. It is of great importance to discuss the Laughlen test because of the claims advanced, namely, that it is reliable and that it does not require a special laboratory but can be performed in the office of every physician.

DR. JACOB CHURG (by invitation): Laughlen claims numerous advantages for his method over the tests now in use. According to him, it is easy to perform, takes from five to ten minutes to complete and, above all, is accurate; the antigen is stable for from seven to ten days and is easily available in emergencies; finally, the test is so simple that no special technical skill is required, and it can safely be placed in the hands of every physician.

Prompted by the claims stated, particularly by the last one, we undertook a study of the test. The equipment for the Laughlen test is simple. All that is required is the antigen, the slides, a couple of pipets and control specimens of serum known to be positive and negative. The antigen is supplied in an inactive form and has to be activated before using. A drop of fresh serum (not inactivated) is placed on a slide, preferably a Kline slide. If the reaction is positive, red clumps form in a previously homogeneous and turbid fluid. These clumps are small at first but gradually enlarge. The fluid loses its color and becomes clear. If this reaction takes place within five minutes, it is considered strongly positive; if it becomes positive between five and ten minutes, weakly positive. Any granulation that appears after ten minutes is considered nonspecific.

Laughlen found that the results of his test agreed with those of the Wassermann test in 98 per cent of cases and with those of the Kahn test in 99 per cent. Robinson and Stroud, who performed this test in 1,000 cases, found that its results agreed with those of the Wassermann test in 93 per cent of cases and with those of the Kahn test in 97 per cent. My associates and I have performed about fifteen hundred tests in the Central Social Hygiene Clinic of the Department of Health, comparing the results with those of routine Wassermann tests. In the cases in which the Wassermann test was negative and the Laughlen test positive, the Wassermann and the Laughlen test were repeated and a Kline test was performed. We followed the technic of the sponsors of the test, but our results indicate that it is far from being accurate, since it agrees with the Wassermann test in only about 70 per cent of the cases. It is clear that of all cases of syphilis in only

50 per cent can the disease be detected by the Laughlen test. The results are influenced to a great extent by antisyphilitic treatment. In cases in which there had been no treatment the results of the Laughlen test agreed with those of the Wassermann test in 85 per cent, and in cases in which treatment had been given, in 50 per cent. This lack of agreement is due almost entirely to the low sensitivity of the test. False positive results were not numerous (about 2 per cent).

Somewhat better results were obtained when we experimented with specimens of serum which had been inactivated by heating (twenty-five minutes at 56 C. [132.8 F.]). The percentage of agreement rose to 75 per cent—60 per cent in cases in which treatment had been given and 90 per cent in cases in which no treatment had been employed. In a series of parallel tests with heated and unheated specimens of serum we encountered a number of syphilitc specimens which gave negative results before inactivation and strongly positive results after inactivation. These results indicate that inactivation is an essential procedure in performing the Laughlen test. Even with inactivated serum, however, the low sensitivity of the test makes it useless for practical purposes.

In conclusion I wish to state that in its present form the Laughlen test is not a reliable procedure and should not be employed. Whether it will prove satisfactory in the future we do not know as yet, but even if it can be improved on, it will probably remain a laboratory procedure. In spite of the simplicity of the test, there are numerous seemingly unimportant details which must be strictly adhered to in order to obtain good results.

DR. NATHAN SOBEL (by invitation): Dr. Churg brought out the important points in connection with this work. As is well known, there are a number of modifications of the Wassermann test as well as precipitation tests, and this fact alone proves that none is entirely satisfactory. Laughlen claims rapid and accurate results. We found that the sensitivity of this test was hardly equal to that of the Wassermann test. Our results did not agree with those of Laughlen or with those of Robinson and Stroud. Regarding the ease and simplicity of this test, Laughlen states that it is an office procedure; yet we found that we had to discard the results in the first 300 tests because we lacked the experience for their accurate performance. In other words, we had to learn how to do the test properly. In a recent country-wide survey regarding Wassermann tests, it was shown that the test employed mattered less than the care taken in performing it, and this applies to the Laughlen test as well. The Laughlen test at the present time is not suitable for use by the average practitioner. It is still a laboratory procedure.

DR. CHARLES R. REIN (by invitation): I was especially interested in the discussion of the new Laughlen test by Drs. Churg and Sobel, because their results are similar to those obtained by Miss C. Hazay in my laboratory. She and I have compared the Laughlen test with other accepted complement fixation and flocculation tests in about 500 cases. So far, our studies have revealed the following facts: 1. Doing the Laughlen test on Kline slides (glass 2 by 3 inches [5 by 7.5 cm.] slides on which are mounted twelve paraffin rings, each with an inside diameter of 14 mm.) improves its results. 2. The results of the Laughlen test with raw serum are unsatisfactory, yielding many false negative reactions. Inactivation of the serum increases the sensitivity. Inactivation at 56 C. for ten minutes or at 63 C. for three minutes is adequate. 3. The Laughlen test with citrated serum gives unsatisfactory results, yielding a large number of false doubtful reactions and even an occasional false positive reaction. 4. The results obtained with the Laughlen antigen emulsion when it is more than six days old are not clearcut and are difficult to read.

I believe that new tests of this type should not be publicized and sold to general practitioners until their specificity and sensitivity are accurately determined by reliable serologists.

DR. LOUIS CHARGIN: The Laughlen test is the latest addition to the present equipment for the serologic diagnosis of syphilis. The thorough and lucid dis-

cussion of the previous speakers makes it clear that as yet the claim cannot be made that the Laughlen test will supersede the Kline, the Kahn and the Wassermann test.

Trichorrhexis Nodosa. Presented by Dr. Samuel Feldman.

C. I., a student aged 22, states that about six months ago he first noticed considerable thinning of the hair. The hair in the region above the temples began to break off about ½ inch (1.3 cm.) above the follicular orifice, giving that part of the scalp the appearance of a freshly mowed lawn. Most of the stumps were brushlike at their broken ends. The nodes on the shafts of the hair are easily seen with a hand lens, but details are easier to study under the microscope.

A Case for Diagnosis (Psoriasiform Eczema? Mycosis Fungoides?). Presented by Dr. Charles A. Greenhouse.

S. F., a man aged 61, was first seen at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Oct. 29, 1937, with an eruption of five years' duration. On the volar surfaces and to a lesser degree on the extensor surfaces of the lower extremities, in the sacral area and on the elbows, there are sharply defined scaly, follicular erythematous patches about the size of a palm; in some of them the patulous follicles have horny plugs. Some of the plaques are crusted, and those at the left ankle and on the left sole are almost typical of psoriasis.

The first histologic examination showed slight acanthosis of part of the epidermis and occasional parakeratosis. Throughout the middle and the upper portion of the cutis the vessels were dilated. There was a partly focal and partly dense infiltrate throughout the entire cutis. The cellular element was composed of small round cells, invading connective tissue cells, plasma cells and histiocytes. Throughout the cellular infiltrate reticulum was seen. There was no clumping or nests of cells in the epidermis. A section from another area showed dilated vessels throughout the cutis and about them a rather marked cellular infiltrate composed of small round, wandering connective tissue cells and an occasional plasma cell and histiocyte. There was some necrosis of the walls of the vessels, and a diffuse cellular infiltrate of fibroblasts in the framework of the cutis. The epidermis was irregularly acanthotic; the basal cell margin was intact. The first histologic examination revealed a picture suggestive of mycosis fungoides, and the second showed perivasculitis.

DISCUSSION

Dr. David L. Satenstein: This patient has various types of lesions. The calves and the inner surfaces of the thighs show plaques which are definitely infiltrated. The absence of itching is irrelevant. I know of patients with mycosis fungoides who never experienced itching. Most of the members will recall the case of Wise and Rosen in which the condition resembled parapsoriasis and microscopically proved to be mycosis fungoides. There was not a single scratch mark on that patient. I was told that in the case of Dr. Greenhouse's patient a number of sections taken from various lesions were studied. The first section showed mycosis fungoides, while the second showed no such evidence. It is, of course, known that occasionally the disease does not manifest itself to such an extent that a positive diagnosis can be made. However, when the tissue becomes "fixed" —if I can use that expression—one can arrive at a definite diagnosis. From the clinical picture and the histologic observations I should call this case one of mycosis fungoides. I admit that some of the lesions lack the characteristics of mycosis fungoides both clinically and histologically, but it is only a question of time until these too will become typical of the disease.

Dr. Frank E. Cross: When one considers the infiltrated patches on the left leg in association with the histologic changes, one is forced to the conclusion that

mycosis fungoides is present. The interesting histologic observation is that the tissue from the infiltrated plaque did not show mycosis fungoides, whereas the section from the noninfiltrated tissue did show typical mycosis fungoides.

DR. PAUL GROSS: In the first place, one has to admit that an apparently typical psoriatic eruption can precede mycosis fungoides. The case presented tonight shows, besides the clinical resemblance to psoriasis, other features which are highly suggestive of that diagnosis: (1) the development of a more acute eruption around the chronic patch of psoriasis, usually due to the transformation of chrysarobin dermatitis into psoriasis, and (2) the appearance of a bandlike border, accompanied with lessening infiltration or clearing in the center to produce geographic designs. Spinulosis, as in this case, may develop in connection with any of a number of cutaneous eruptions, either spontaneously or from follicular irritation by ointments. Therefore, one should make the clinical diagnosis of psoriasis and leave it to the histopathologist to supply the proof for the diagnosis of mycosis fungoides.

DR. ARTHUR SAYER: I believe that the latest literature on mycosis fungoides has been more or less emphatic on the point that clinically one cannot make an absolute diagnosis of mycosis fungoides in a great many cases, and in numerous instances the diagnoses has to be changed subsequently, as the clinical picture alters. Then, too, in cases in which autopsy is performed the diagnosis is sometimes proved to be wrong.

Clinically one often confuses mycosis fungoides with Hodgkin's disease, leukemia or parapsoriasis, and a complete study, including biopsies and repeated blood counts, is necessary. I think that a definite diagnosis cannot be made in this case at present. Further observation is necessary.

DR. DAVID L. SATENSTEIN: It is known that an eruption clinically regarded as eczema or psoriasis may turn out to be mycosis fungoides. Any inflammatory process that persists in the cutis for a long time can cause changes that make one suspect tuberculosis, leprosy or mycosis fungoides. Dr. Gross calls attention to a plaque's showing an infiltrated margin and a less active center and regards that as characteristic of psoriasis. I think the presence of such plaques is a pretty good indication of mycosis fungoides and not of psoriasis. The keratosis and follicular plugging in this patient are not uncommon in cases in which local treatment has been employed.

DR. CLINTON H. MARTIN: The patient states that some of the patches disappeared spontaneously. This is not a common occurrence in cases of mycosis fungoides, but it occurs frequently in cases of psoriasis. That is a point which might help to differentiate between mycosis fungoides and psoriasis in this case.

DR. CHARLES WOLF: The clinical features, the duration and the histologic picture suggest the diagnosis of a psoriasiform type of prefungoid mycosis fungoides. The patient should be given roentgen treatment; if the eruption is mycosis fungoides, it should resolve rapidly.

DR. LOUIS CHARGIN: I agree with Dr. Satenstein that one cannot make a definite clinical diagnosis of mycosis fungoides. The eruption that this patient presents is largely psoriasiform, but there are areas that resemble pityriasis rubra pilaris. Dr. Satenstein states that some parts of the tissue show mycosis fungoides histologically while other areas do not. I believe that there is a stage of prefungoid mycosis fungoides in which the histologic picture is not that of mycosis fungoides. There is general agreement that once one finds tissue of mycosis fungoides in one area, all the areas will show a similar structure.

In favor of mycosis fungoides in this case is the lack of uniformity in the infiltration of the plaques, to which Dr. Fox has often called attention.

DR. CHARLES A. GREENHOUSE: The reason for presenting this patient was to stress the discrepancy in the pathologic report; the diagnosis of mycosis fungoides was not accepted by all those who examined the slides. My feeling is that at least clinically the case is one of psoriasis that has been improperly treated.

A Case for Diagnosis (Rosacea-Like Tuberculid of Lewandowsky?). Presented by DR. SAMUEL FELDMAN.

J. C., a man aged 44, states that he acquired syphilis about ten years ago. He was treated regularly until 1935. The present eruption appeared about seven months ago and has shown several remissions. On the forehead, the chin and the nose are papulopustules the size of a pinhead and larger. There is no telangiectasia.

Histologic examination of sections taken from a papulopustular lesion showed the epidermis of the central portion to be entirely missing. The epidermis of the edges was edematous, partly necrotic and invaded by polymorphonuclear leukocytes. Immediately below the denuded area was a circumscribed mass of infiltration, mostly of round cells, with some plasma cells and a number of polymorphonuclear leukocytes. There was no evidence of granulation tissue.

DISCUSSION

DR. MARION B. SULZBERGER: There are several diagnoses to be considered in this case. One is of a type of tuberculid, as Dr. Feldman suggests. There is no grouping and no agmination of these rather large papular lesions. They are discrete and irregularly disseminated over the face. There is no tendency to confluent erythema. Most of the lesions are too large for rosacea-like tuberculid, and there is no telangiectasia. Moreover, the distribution is not primarily on the cheeks or the forehead, but the lesions are fairly regularly disseminated over the face. For these reasons I think lupus miliaris faciei is a more probable diagnosis. However, other conditions can produce such a picture, for instance, iododerma or bromoderma. There is a remote possibility that this case may be one of atypical tuberculosis papulonecrotica of the type of acnitis.

DR. CHARLES WOLF: My diagnosis is rosacea. In cases of lupus miliaris or of Lewandowsky's rosacea-like tuberculid one finds more infiltration than is present in this case. The presence of itching and of various types of lesions can be considered in favor of rosacea.

DR. SAMUEL FELDMAN: I cannot agree with Dr. Wolf that this case is one of ordinary rosacea. The diagnosis rests between rosacea-like tuberculid of Lewandowsky and lupus miliaris disseminatus faciei, suggested by Dr. Sulzberger.

Cheilitis Exfoliativa. Presented by DR. SAMUEL FELDMAN.

C. C., a housewife aged 26, born in Russia, states that about eight months ago her lips became swollen and painful and began to exfoliate. At times a scaly cast of the entire lip could be removed. Roentgen treatment brought no apparent relief. At present the skin and the mucous membrane of the lips appear thin and shiny.

DISCUSSION

DR. MAURICE UMANSKY: The cheilitis of this patient may be of actinic origin. She states that the condition appeared in midsummer and improved with the approach of fall. Cosmetics applied to the lips may have acted as a sensitizer to light. The patient shows definite gingivitis and pyorrhea, which are considered etiologic factors in cheilitis. Treatment of the gingivitis may therefore benefit her.

DR. MARION B. SULZBERGER: Dr. Joseph Goodman and I have studied a relatively large series of cases of cheilitis in women and presented a paper on the subject before the American Dermatological Association (ARCH. DERMAT. & SYPH., to be published). In all but two cases we demonstrated that the cause was one or more ingredients of lipstick. In our series it was easy to determine the blameworthy ingredient when the reactions to patch tests were positive. However, there were four cases in which repeated patch tests with lipstick gave negative results, and in these it was only by elimination and reexposure that we were able to come to definite conclusions. Our procedure was as follows: The lipstick was eliminated, and when the cheilitis cleared (this sometimes took as long as six weeks)

the patient was told to apply the suspected lipstick. If this caused a prompt recurrence, we considered that this proved the cause of the cheilitis. We then proceeded in the same manner with each of the different ingredients of the lipstick. This is, of course, a clumsy, tedious, difficult form of investigation, but it is necessary if one wishes to ascertain the causal ingredient. An interesting point is that practically all lipsticks used today are "indelible" and to this end contain derivatives of tetrabromofluorescein. In this connection it is most interesting to recall that dyes of this group (for example, eosin) are photosensitizing agents, and indeed photosensitization played a demonstrable role in some of our cases of lipstick cheilitis.

I must emphasize, however, that I do not mean to say that cheilitis in all cases is due to lipstick. In some it may be due to gingivitis, to other irritants or to photosensitization. Nevertheless, the cases of women which we were able to study in the city of New York showed that the most frequent cause was lipstick.

DR. SAMUEL FELDMAN: I am extremely grateful to Dr. Sulzberger for having brought to the members' attention the etiologic role of lipstick. I experimented with lipstick with this patient but could not demonstrate sensitivity to the brand she used; patch tests with her lipstick invariably gave negative results. It is not likely that a mouth wash or a dentifirice is the cause, as such substances have not been used recently.

Sarcoid of Boeck. Presented by DR. DAVID BLOOM.

S. S., a man aged 52, was seen first in 1931, when he had lesions on the face which were diagnosed as sarcoid of Boeck. In 1933 he was referred to a general radiologist for superficial roentgen therapy. When reexamined, the patient stated that for the past several years he had received radium treatment at intervals of from one to several weeks.

The patient presents on the forehead irregularly shaped erythematous, somewhat raised plaques which have not been exposed to radiation. Underneath the left eye there is an oval depigmented telangiectatic lesion, and on the left cheek there is an erythematous plaque with a crust in the center, which is the result of exposure to radiation.

The family and personal history were irrelevant. The intradermal tuberculin test gave a moderately positive reaction with a dilution of 1 : 100,000 and a strongly positive one with a dilution of 1 : 1,000. The Wassermann reaction of the blood was negative. The blood count revealed 3,370,000 erythrocytes, 5,800 leukocytes and 66 per cent hemoglobin. The differential count was normal.

DISCUSSION

DR. MARION B. SULZBERGER: I think Dr. Bloom should be commended for presenting this case. The point which he wishes to illustrate is important to all the members. We should let it be known that dermatologists are best equipped to treat, or to direct the treatment of, cutaneous diseases. There are many special fields in medicine, and these are divided according to a variety of criteria. We are dermatologists because we specialize in conditions of the skin; our specialty is one based on the criterion of the organ affected. Pediatrics is a specialty based on the age of the patient, no matter what the patient's complaint is. Radiology in turn is based not on the organ affected or on the age of the patient but on the modality employed. Endocrinology is based not on the organ affected, the age of the patient or the modality employed but on an interrelated functional system. Allergy is delimited not by organ, age, modality or functional system but by the inclusion of a certain group of related biologic phenomena. Both syphilology and the specialty of cancer are founded on still another basis, namely, that of a specific disease entity. It is therefore self evident that there will be much overlapping, due to the fact that the classification of specialists is not on a uniform basis, and it is, therefore, up to dermatologists to make clear that it is in general essential that cutaneous conditions be treated by dermatologists. Of course, one

is forced occasionally to consult with other specialists, such as radiologists, who have no experience in dermatologic diagnosis; guidance and advice often lead to unfortunate results and should therefore be deprecated. Not only are the dermatologic knowledge and experience of radiologists usually insufficient for dermatologic problems, but their equipment is almost always inadequate for the best dermatotherapy.

DR. DAVID L. SATENSTEIN: One of the chief difficulties encountered in general hospitals is that these institutions do not equip the department of dermatology to do comprehensive work. Thus, a patient presenting a condition calling for a minor surgical procedure must be referred to the surgical department; similarly, roentgen therapy is carried out independently by the department of radiotherapy. All that seems to be left to the dermatologic department is to write prescriptions and refer the patients to other departments. Accidents such as this occur less frequently in institutions in which the dermatologic department is self sufficient.

DR. CHARLES LERNER: I do not wish to appear in the role of a reformer. It seems to me that it would be of benefit to patients and to dermatologists, as well as to clinics and hospitals, if the dermatologists would direct the superficial roentgen therapy.

DR. DAVID BLOOM: Dr. Sulzberger brilliantly illustrated the purpose of presenting this patient. Again and again one sees patients whose skin has been injured by treatment administered by general radiologists. It seems as if general radiologists, in a desire to cure a cutaneous lesion, often show little regard for the consequences of excessive irradiation. It is obvious that this incorrect treatment is due to the poor knowledge of dermatologic lesions on the part of the general radiologist and to his ignorance of the well established technic of irradiation in dermatologic practice. It is therefore necessary that the dermatologic department should have its own facilities for irradiation to avoid the harm now done to patients by such overzealous treatment on the part of general radiologists. The American Board of Radiology would do a service to the patient if it would request radiologists to be well acquainted with the technic of irradiation in dermatologic practice or to treat cutaneous diseases only under the direction of a dermatologist.

Report on a Case for Diagnosis (Folliculitis Sycosiformis Atrophicans?) in a Syphilitic Patient. Presented by DR. HENRY SILVER.

U. S., a man aged 56, was presented at the meeting of the Bronx Dermatological Society on Oct. 28, 1937.

DISCUSSION

DR. HENRY SILVER: There was considerable disagreement at the previous presentation as to whether the eruption was syphilis per se or a sycosiform eruption in a syphilitic patient. It was suggested that more intensive antisyphilitic treatment be given. Accordingly, the patient has received three injections of arsphenamine and eight of bismuth subsalicylate. The eruption shows marked improvement on the left side.

DR. DAVID L. SATENSTEIN: The presence of plasma cells in the section does not necessarily mean syphilis, because one finds plasma cells in association with many diseases. I suggest the diagnosis of ulerythema ophryogenes. If this patient had lesions on the eyebrows in addition to those at the hair line, no one would question that diagnosis.

DR. ARTHUR SAYER: I think that the therapeutic test should be considered final in cases of doubtful syphilis. If the lesions heal while the patient receives antisyphilitic treatment, that is almost final evidence that the lesions are of syphilitic origin. Conversely, the failure of the lesions to respond to sufficient antisyphilitic treatment must be considered as strong evidence of the nonsyphilitic nature of the lesion.

DR. DAVID L. SATENSTEIN: I do not agree with Dr. Sayer's remarks. Improvement under antisyphilitic therapy does not necessarily stamp the lesion

as syphilis. Sarcoid and lupus erythematosus improving under therapy with a bismuth preparation furnish examples.

DR. LOUIS CHARGIN: I certainly cannot agree that the amount of improvement shown by this patient corresponds to that seen in a successful therapeutic test. Last month I stressed the point that with a patient who had not had prior antisyphilitic treatment rapid improvement would ensue in a week or two. This patient has had treatment for about eight weeks, and the eruption has not yet disappeared. I admit that the left side is considerably improved.

DR. PAUL GROSS: When this patient was presented a month ago, I favored the diagnosis of syphilis. The response to treatment to date is disappointing, and I believe that the condition belongs in the group of chronic folliculitis.

DR. FRANK E. CROSS: Is it not a fact that follicular infections usually are resistant to any form of treatment? If this condition is folliculitis sycosiformis atrophicans, it seems to me to have responded faster than usual.

DR. HENRY SILVER: Folliculitis decalvans, or folliculitis sycosiformis atrophicans, spreads rapidly into the hairy scalp, but this eruption remained strictly limited to the hair line. I know that Dr. Bloom has studied this subject, and I should be interested in hearing whether he has seen eruptions limited to the hairline.

DR. DAVID BLOOM: It is my impression that the clinical picture presented by this patient is definitely one of folliculitis sycosiformis atrophicans and has no connection with his syphilitic infection. The conspicuous features in this patient consist of alopecia along the hair line in a skin suggesting scarring, a narrow strip of folliculitis along this area and a patch of alopecia on the left temple. The presence of plasma cells histologically does not speak against this diagnosis. On the contrary, Hoffmann, who has described this clinical entity, emphasizes the presence of plasmoma in the tissue. Involvement of the scalp may be mild, and the absence of folliculitis in this area does not speak against the diagnosis.

Disseminated Lupus Erythematosus. Presented by DR. SAMUEL FELDMAN.

K. K., a housewife aged 40, born in Ireland, states that in July 1937, after exposure to the sun, she noticed the appearance of red blotches, accompanied with itching of the face, the chest and the forearms. When she was subsequently exposed to the sun, the itching and erythema became aggravated.

On the forehead, the cheeks, the nose, the upper lip, the area below the ears, the upper portion of the chest and the anterior surfaces of both forearms there are a number of slightly infiltrated erythematous patches. On the face the lesions show definite dilatation of the follicles and an almost imperceptible scaliness. All the other patches are more or less smooth and practically devoid of scales.

Urinalysis and examination of the blood, including the Wassermann test, showed no abnormality. The tuberculin test elicited a positive reaction with a dilution of 1:1,000,000. A roentgenogram of the chest revealed no abnormalities.

Sections were taken for microscopic study from the right mandibular region and from the left forearm. The skin in both those places was rather smooth and not scaly and showed no clinical evidence of follicular dilatation. The epidermis in most places consisted of six layers of cells and in some places was thinned to about three layers. The hair follicle was dilated and filled with a horny plug. The rete showed mild hyperkeratosis and edema. There were vascular dilatation and marked perivascular infiltration in the cutis and in the papillary layer. The collagenous bundles appeared to be thicker and somewhat homogeneous. The elastic fibers were not diminished; they appeared rather thick, and there was a certain amount of clumping. The section from the forearm showed edema, vascular dilatation and perivascular infiltration. The elastic tissue appeared normal.

DISCUSSION

DR. DAVID BLOOM: I am certain that Dr. Feldman is aware that one has to be cautious in the administration of gold preparations in cases like this. Several

patients under my observation have shown a marked exacerbation of the eruption after the administration of as little as 10 mg. of sodium gold thiosulfate. Bismuth preparations are indicated in cases like this.

DR. FRANK E. CROSS: While I am inclined to agree with the diagnosis, one has to regard this condition as a subacute type of lupus erythematosus disseminatus. The patient's well being speaks against acute lupus erythematosus. Therefore, therapy with a gold preparation may be given cautiously. Because of the history of the eruptions following exposure to sunlight, the therapy should include proper protection of the face at all seasons.

DR. SAMUEL FELDMAN: I am still in doubt as to whether this condition is the acute type of the disease. On the cheeks there are two patches which show a little scaling, and there are dilated follicles with horny plugs. These features make the picture fairly typical of the discoid type of lupus erythematosus. On the arms, however, the picture is that of multiform erythema. The sections taken from the face show lupus erythematosus histologically, but the sections from the arm do not. It is difficult to predict whether the eruption will ultimately be the fixed or the acute form of lupus erythematosus.

Lichen Nitidus. Presented by DR. SAMUEL FELDMAN.

L. D., a school girl aged 11 years, states that about two months ago an eruption appeared in the form of patches on one arm and then spread to other parts of the body. Each patch is made up of whitish flat shiny papules no larger than a pinpoint; these do not scale. On the back and the front of the thighs there are a large number of discrete and somewhat horny papules which are not grouped.

The tuberculin test with dilutions of 1:1,000, 1:10,000 and 1:100,000 gave negative results. The examination of the chest showed no abnormality.

DISCUSSION

There was unanimous agreement with the diagnosis.

Leukoplakia and Interstitial Glossitis. Presented by DR. ARTHUR SAYER.

Psoriasis Vulgaris with Glovelike Distribution. Presented by DR. LOUIS CHARGIN.

CLEVELAND DERMATOLOGICAL SOCIETY

CLAUDE BAZIL NORRIS, M.D., *President*

Sept. 30, 1937

C. L. CUMMER, M.D., *Secretary*

J. R. DRIVER, M.D., *Reporter*

A Case for Diagnosis. Presented by DR. E. W. NETHERTON.

G. D. S., a man aged 27, for the past two years has had a red scaly pustular eruption on the scalp and the bearded portion of the face. Roentgen treatment produced temporary improvement in the eruption. Salves also produced some benefit.

A brother had acne, his father chronic rheumatism and his mother cardiac disease. There has been no tuberculosis in the family.

In March 1937 a number of small, slightly pruritic "pimples" appeared over the anterior portion of the chest. Since then groups of new lesions have continued to develop over the trunk, the scrotum, the penis, the face and the neck and to some extent on the extremities.

Examination shows the following types of cutaneous lesions to be present:

1. A diffuse erythematous scaly pustular eruption on the bearded portion of the face. The pustules are small and follicular.

2. A papular eruption involving the face, the neck, the ears, the chest, the abdomen, the upper portion of the back, the lumbar region, and the upper portion of the extremities. The papules vary in size from that of a pinhead to that of a match head, are round and globular and vary in color from that of the skin to a pinkish brown. Some lesions are umbilicated. The smaller lesions are smooth. Most of the papules are discrete. However, some groups are confluent. The larger papules are surrounded by a narrow zone of hyperpigmentation. A granulomatous infiltration can be observed by diascopic examination.

3. A few round flat dime-sized erythematous crusted lesions on the chest. The crusts are thin and adherent. These lesions have developed within the past two weeks.

4. Some lichenification of the skin on the lateral surface of the left leg.

Roentgen examination of the chest showed no abnormality. There were 4,003,000 red blood cells and 8,700 leukocytes. The differential count was normal. The Wassermann and the Kahn test were negative. A tuberculin (Mantoux) test with a dilution of 1:10,000 gave negative results.

Biopsy of an early lesion, a small papule, showed the surface of the epidermis to be covered with a layer of parakeratotic cells. There was acanthosis at the border of the papule, while the epidermis on the surface of the lesion was thin. There were intracellular and intercellular edema of the cells of the rete mucosa and destruction of many cells. A moderate amount of lymphocytic invasion was present in the epidermis. In the corium there was a well defined loose cellular infiltrate in the papillary and the subpapillary layer. There were few lymphocytes in the infiltration, which consisted mainly of epithelial cells and fibroblasts. There were no eosinophils, plasma cells or giant cells. There was considerable edema, with dilatation of the vessels in the papillary layer. An old lesion showed essentially the same changes, except that acanthosis was more marked and most of the corium was involved. There was loose edematous stroma throughout the infiltration.

DISCUSSION

DR. H. N. COLE: While this suggestion seems a little irregular, I do not see why this condition could not be explained as sycosis vulgaris with a secondary infectious eczematoid dermatitis. There is no question but what the condition on his face could be diagnosed as sycosis vulgaris. Those patients often get lesions on other parts of the body. I think the other lesions are infectious eczematoid dermatitis.

DR. J. EDGAR FISHER: In his type of work in the brickyard the patient comes in contact with zinc and lead. Do you feel that these have any influence?

DR. E. W. NETHERTON: Those factors were considered, and it was felt that since he worked in a brickyard with brick dust, he might have some silicosis, but he shows no signs of that. He does not have the dermatitis usually seen in cases of dermatitis venenata. The lesions are discrete and papular, with some confluence. There is a little itching—but not a great deal. Certainly the lesions are not markedly excoriated.

DR. C. G. LA ROCCO: Examination of the lesions on the trunk shows that they certainly are not pustular but firm. I cannot accept the suggestion that this condition is an infectious eczematoid dermatitis.

DR. E. W. NETHERTON: I do not know what this patient has. Several possibilities have been considered. For the eruption on his scalp, and especially on his face, sycosis vulgaris was thought of. The eruption clears when chlorhydroxyquinoline ointment is applied and as long as that is used remains in pretty good shape. The patient has had numerous pustules, of which only a few are present today. The scalp was covered with an oily type of scale, a good deal like

seborrheic eczema. The lesions on his body were somewhat larger and at first a little more dome shaped. Clinically, the condition was considered to be molluscum contagiosum, but no molluscous bodies could be expressed, and the biopsy ruled the diagnosis out. Infectious eczematoid dermatitis ought to be considered, although he has no vesicles and few pustules, but he has eczematoid lesions on the breast that have appeared since he was seen two weeks ago.

DR. J. EDGAR FISHER: There are some pustular lesions on the patient.

Paget's Disease of the Nipple. Presented by DR. GARRETT ARTHUR COOPER (from the Department of Dermatology and Syphilology, the Lakeside Hospital).

M. G., a housewife aged 51, has a sore on the right nipple which developed after a human bite three years ago. The lesion has slowly enlarged and now is sensitive to heat and cold.

On the nipple and the areola of the right breast there is a somewhat beefy, red weeping lesion with a sharply defined border. It is slightly elevated and infiltrated but apparently limited to the skin. The axillary nodes are not palpably enlarged.

Radical surgical amputation of the breast has been advised.

A biopsy on September 18 showed one edge of the section to have an intact layer of well keratinized stratified squamous epithelium. In the middle portion were a number of Paget cells. Intracellular bridges were not seen. There were mitotic figures and an infiltration of eosinophils.

DISCUSSION

DR. H. N. COLE: I was interested in the pathologist's report in this case. There was a diagnosis of squamous cell carcinoma. It seemed to me that one could find the typical Paget cells, and mitotic figures showing the direct and the indirect type of division were present. Histologically, I thought the picture was compatible with Paget's disease, and certainly clinically the patient has Paget's disease. I feel from a study of the section that a diagnosis of squamous cell carcinoma of the breast would be more difficult to make than one of Paget's type of carcinoma.

Sickle Cell Anemia Associated with Ulcers on the Legs. Presented by DR. W. F. SCHWARTZ (from the Department of Dermatology and Syphilology, the Cleveland City Hospital).

D. J., a Negress aged 12, was admitted to the Cleveland City Hospital on Aug. 16, 1937. She complained of ulcers on the right leg, associated with vague aches in the back and the legs of two weeks' duration.

One ulcer was located on the anterior aspect of the middle third of the right leg. A punched-out and sharply demarcated area 1 cm. in diameter had somewhat elevated borders and a relatively clean base and was covered with a moderate amount of dried serous discharge. There was a similar type of ulcer on the upper part of the right leg anteriorly. This was surrounded by a moderate amount of erythema and swelling. At present the ulcers have completely healed, leaving depressed scars.

At the time of examination the scleras and the mucous membranes of the eyes and the mouth showed marked pallor. There was a loud systolic murmur at the base of the heart. Serologic tests for syphilis gave negative results, as did the tuberculin test. The erythrocytes ranged between 2,200,000 and 2,600,000; there were 16,000 leukocytes and 60 per cent hemoglobin (Tallqvist); the color index was 1.28, and there were 56 per cent polymorphonuclears, 6 per cent small mononuclears, 25 per cent large mononuclears, 6 per cent monocytes and 7 per cent eosinophils. On Aug. 27, 1937, 95 per cent of the red cells showed sickling after eighteen hours, but on Sept. 21, 1937, only an occasional sickle cell could be demonstrated. The reticulocyte content increased from 1 per cent at the time of admission to 7.2 per cent ten days after liver therapy was instituted. Smears of blood showed sickling of the red cells.

Medication consisted of 1 cc. of concentrated liver extract intramuscularly four times a day for twenty days and 5 grains of saccharated ferrous carbonate three times a day.

DISCUSSION

DR. E. W. NETHERTON: The smears of blood presented show beautifully the sickling of the red cells. This case is similar to one I presented before this society several years ago, in which a Negro had an ulcer on the ankle (ARCH. DERMAT. & SYPH. **34**:158 [July] 1936). I have seen the patient in recent months, and the ulcer has remained unhealed. In my experience it has been extremely difficult to heal these ulcers. Did the liver therapy have any influence on the sickling of the red cells?

Dr. W. F. SCHWARTZ: About three weeks after therapy with liver and iron was started, sickling of the cells almost disappeared. The number of red blood cells did not increase much, however.

DR. S. C. BOWEN: In the south, where this condition is common, it has been found that the response is better to repeated small blood transfusions than to liver.

DR. EDWARD STEINBERG: Is the condition limited to Negroes?

DR. E. W. NETHERTON: While sickle cell anemia is usually seen in Negroes, it is found occasionally in other races. My associates and I have observed two cases in Italian sisters.

DR. W. F. SCHWARTZ: Before the examination of the blood for sickling it has been found that the saline suspension of cells should stand for approximately eighteen hours.

A Case for Diagnosis (Spiegler-Fendt Sarcoid? Leukopenic Leukaemia Cutis?). Presented by DR. E. W. NETHERTON.

I. F., a white woman aged 32, had a pigmented mole excised from the forehead in July 1933. Two years later a "cyst" was removed from the posterior fold of the left axilla. In August 1937 she underwent dilation, curettage and excision of rectal papillae. At the same time a few moles on the face and the neck were removed with the electric cautery. In 1935 the patient had a pruritic eruption which was probably urticarial.

About a year ago a thickened, slightly itchy red area appeared on the left shoulder. This has enlarged gradually. Within the past few months similar lesions have appeared on the right arm, on the face and on the right leg. These lesions have enlarged gradually, and there has been slight itching.

There is no enlargement of the spleen or the superficial lymph glands. General physical examination showed no abnormality.

On the lateral and the extensor surface of the right arm are a few dull red smooth, infiltrated plaques and nodules, confined to the skin.

Roentgenograms of the chest showed no abnormality. The Mantoux test with 0.05 cc. of a dilution of 1:1,000 of old tuberculin gave strongly positive results. Routine blood and differential counts gave results within normal limits. The Wassermann reaction was negative.

Histologic examination showed the epidermis to be intact and without abnormality. Throughout the corium there were dense, sharply demarcated collections of well differentiated lymphoid cells. There were hyperplastic germinal centers at the central portion of each area of cellular infiltration and numerous small collections of lymphocytic infiltration around the blood vessels.

DISCUSSION

DR. H. N. COLE: This case is extremely interesting. The number of lesions would speak more in favor of Spiegler-Fendt sarcoid than of leukaemia cutis, and yet the microscopic picture suggests leukaemia cutis. A number of years ago I reported a case as one of leukosarcoma. The picture presented by this patient microscopically is the exact replica of that in my case, but in my case

there were hundreds of lesions. Within a few months my patient died, while the patient presented today has a process that seems slow in spreading, and there is nothing at all acute about it. If it were not for these factors, I should prefer a diagnosis of leukaemia cutis. There have been one or two cases of a monocytic type of leukemia reported recently which resembled this case.

DR. R. E. BARNEY: In this particular case one of the lesions just above the elbow suggested granuloma annulare. Histologically, however, the picture was not consistent with a diagnosis of granuloma annulare.

NOTE.—All the lesions disappeared after fractional doses of roentgen radiation filtered with 1 mm. of aluminum. Blood counts have remained normal.

Kaposi's Varicelliform Eruption (Dermatitis Gangraenosa Infantum). Presented by DR. W. F. SCHWARTZ (from the Department of Dermatology and Syphilology, the Cleveland City Hospital).

E. P., a well developed and well nourished girl aged 7 months, has had eczema of the face and the cubital fossae since she was 2 months of age. The eczema developed after a change from a diet of breast milk to one of skimmed cow's milk supplemented by vegetables. Two weeks ago a vesicular eruption developed on the areas of eczema on the face and the arms. This was associated with fever.

Six days ago the patient was admitted to the hospital, and at this time there are numerous seropurulent vesicles and some small punched-out umbilicated ulcers about 3 mm. in diameter, chiefly on the face, but also on the scalp and in the cubital fossae. The skin of the face is eczematoid, red and considerably swollen.

The temperature ranged between 39 and 40.5 C. (102.2 and 104.9 F.). The child was restless and appeared ill. Examination of the ears, general physical examination and routine examination of the urine showed no abnormality. The erythrocyte count was 3,500,000, the leukocyte count 7,700 and the hemoglobin content 70 per cent.

Cultures of material aspirated from unbroken vesicopustules showed Staphylococcus aureus. Cultures of blood revealed solutions of the same organism.

Treatment consisted of compresses soaked with boric acid and of potassium permanganate. Manson's lotion was applied to the lesions, and a clysis of Ringer's solution was given. The condition of the patient has become progressively worse.

DISCUSSION

DR. H. A. HAYNES: I should like to inquire whether there is any history of contact with other children or adults who have been vaccinated. I assume that the baby has not been vaccinated.

DR. W. F. SCHWARTZ: There has been no contact with vaccinated persons, and the baby has not been vaccinated.

DR. J. R. DRIVER: The patient is sick, and some features of the condition suggest impetigo. I believe the use of sulfanilamide would be justified in such a case, particularly since medication thus far has failed to check the disease.

DR. H. N. COLE: I feel that sulfanilamide is being used too much, and in view of the fact that a streptococcus has not been demonstrated, it would not be justified here.

DR. EMERSON GILLESPIE, Canton, Ohio: I favor a diagnosis of impetigo superimposed on eczema.

DR. R. E. BARNEY: I believe this condition is a form of impetigo contagiosa.

DR. E. W. NETHERTON: Two groups of cases of this type were reported recently, by A. D. McLachlan and M. Gillespie (Kaposi's Varicelliform Eruption: An Epidemic of 16 Cases, *Brit. J. Dermat.* **48**:337-356 [July] 1936) and W. Herbert Brown (Kaposi's Varicelliform Eruption, ibid. **46**:1 [Jan.] 1934).

DR. W. F. SCHWARTZ: My associates and I have felt that we may be dealing with a form of impetigo in this case, but the eruption fits almost exactly the description given by Kaposi and that given in the British article referred to by

Dr. Netherton. So far as I know, no cases of this disease have been reported in the American literature.

NOTE.—The patient died three days later. Autopsy and biopsy were not permitted.

Moeller's Glossitis. Presented by DR. CLAUDE BAZIL NORRIS, Youngstown, Ohio.

Mrs. W. C. L., a white woman aged 53, was first seen by me on Aug. 3, 1937, when her chief complaint was of sores in the mouth and on the tongue since December 1934. Previous treatment by her family physician, Dr. C. M. Askue, of Youngstown, Ohio, had consisted of various measures for Vincent's infection. On the supposition that pernicious anemia was the cause of the trouble, liver extract intramuscularly and intravenously had been tried. Stomach U. S. P. was given by mouth in addition to vitamin therapy of various kinds. All therapy, including local applications of small doses of radium by the presenter, has been of no avail. During the past year the discomfort has become progressively worse.

Located on the sides of the tongue and on the buccal mucosa there are several sharply defined red weeping, superficially eroded patches, some of which are covered with a loosely adherent grayish membrane. The papillae over the tongue appear normal.

Gastric analysis showed no marked abnormality. The erythrocyte count was 5,080,000, the leukocyte count 13,250 and the hemoglobin content 90 per cent. Urinalysis showed heavy traces of albumin, much mucus and occasional large and small casts. Serologic tests for syphilis were negative.

Biopsy of a section of the tongue showed extensive erosion of the surface, with vascular granulation tissue replacing the epithelial covering. Occasional islands of from one to three layers of epithelial cells were found over the surface. Part of the eroded surface was covered by a pseudomembrane of fibrin and a few leukocytes. The inflammatory zone had a cleancut border, and beneath this zone was normal-appearing lingual structure. The more active zone of inflammation was superficial, and between it and normal tongue was a zone of dense fibrous tissue showing only rare leukocytes. Above the dense fibrous zone was much looser, more edematous and more vascular connective tissue, infiltrated by an enormous number of lymphocytes and plasma cells and a few polymorphonuclear leukocytes. A thick section gave the appearance of lymphoid tissue. The capillary spaces with widest lumens were most superficial, and the denser accumulation of small round cells lay between the superficial lacelike vascular zone and the deepest dense fibrous zone.

DISCUSSION

DR. BENJAMIN LEVINE: This patient has no teeth. She has been wearing plates which contain considerable rubber treated with a red dye made with mercuric sulfide. The condition might be mercurial dermatitis or stomatitis from her plates.

DR. EMERSON GILLESPIE, Canton, Ohio: I questioned her in regard to the plates. She has had the same plates for seven or eleven years, and the eruption has been present only a short time. From the history I doubt that the eruption could be due to the plates.

DR. C. M. ASKUE, Youngstown, Ohio (by invitation): She has been unable to wear her plates for the last year. In the beginning she wore them just for the cosmetic effect but could not wear them when eating. She would wear them occasionally when she went out.

DR. H. N. COLE: Moeller's glossitis is a rare condition. However, on account of the bright red color and the extreme pain and tenderness, I should agree with the diagnosis. This condition was described when little of the present knowledge of deficiency diseases was available, and it may be that it will be classified differently within the next ten or fifteen years. I remember a case I observed in which it was found that the patient had tapeworms from eating fish. I think that possibility should be looked into, so as to rule out that type of anemia. The disease is intractable from the standpoint of treatment.

DR. J. R. DRIVER: The lesions look like Moeller's glossitis, but I think one would have to consider the possibility of lichen planus. There are some features, particularly on the inner surfaces of the lips, suggestive of lichen planus, and it is known that in severe lichen planus of ten months' duration there is much discomfort. As treatment of Moeller's glossitis is unsatisfactory, it seems to me that injections of a bismuth preparation should be given a therapeutic trial.

DR. R. E. BARNEY: I thought of the possibility of lichen planus, and I do not think any of the features present are against that diagnosis. In cases in which the involvement is severe one finds erosion. There was a definite mosaic network on the tongue and on the lips. On the right forearm were two lesions, one of which, at about the middle of the extensor aspect, was distinctly infiltrated, elevated and violaceous. The other lesion was somewhat above and not so characteristic. I think the diagnosis of lichen planus should be seriously entertained.

DR. H. J. PARKHURST, Toledo, Ohio: I agree with the previous discussions, but I feel that the possibility of a monilial infection should be considered, since the lesions are rather extensive for lichen planus.

DR. J. EDGAR FISHER: I suggest a biopsy of one of the lesions on the arm. That should decide the question concerning lichen planus. The condition looks to me more like Moeller's glossitis. Even the color is against lichen planus of the mouth.

DR. CLAUDE BAZIL NORRIS, Youngstown, Ohio: The section from an oral lesion which I have presented today shows no evidence of lichen planus.

Leukaemia Cutis (Myeloblastic). Presented by DR. E. W. NETHERTON, for DR. R. L. HADEN.

G. S. G., a tall, thin, well developed but poorly nourished boy aged 19, first noticed tender, enlarged glands in the right groin and axilla two months ago. Shortly afterward his abdomen began to enlarge. Three weeks ago an eruption began to appear on the abdomen, the chest and the thighs. The "lumps" in the skin are tender and itch slightly. He has lost about 5 pounds (2.3 Kg.) during the past year and has noticed gradually increased weakness and fatigue. There has been no epistaxis, bleeding from the gums or urinary disturbance.

Disseminated principally over the anterior surface of the trunk and the lower extremities are discrete lesions varying from a few millimeters to 10 cm. in diameter. Most of them are nodular and involve both the subcutis and the skin. The younger lesions are light brown and not raised. The older ones are elevated and bluish purple.

The spleen was enlarged almost to the umbilicus, and the liver was enlarged 3 fingerbreadths below the right costal margin. There was a moderate generalized superficial enlargement of all the lymph nodes except the epitrochlear and popliteal nodes.

A roentgenogram of the skull showed a normal sella turcica. About the outer third of the left sphenoid ridge was a calcific deposit that would make one suspicious of a tumor. Roentgenograms of the chest showed the pulmonary fields and the heart to be normal. There were 2,220,000 erythrocytes with slight pallor, marked anisocytosis and poikilocytosis and an occasional erythroblast. Examinations of the blood gave the following results:

Date	9/ 2/37	9/20/37	9/24/37
White blood cells per cu. mm	7,750	6,000	1,750
Neutrophils, per cent	10	23	37
Lymphocytes, per cent	8	13	24
Myelocytes, per cent	1	2	..
Myeloblasts, per cent	30	58	32
Fragile leukocytes, per cent	51	..	..
Eosinophils, per cent	..	1	4
Monocytes, per cent	..	3	3
Icterus index	4	..	..

Urinalysis showed no abnormality, and serologic tests were negative.

Biopsy showed the epidermis to be intact and without abnormality.

Some of the pilosebaceous follicles were dilated and contained hyperkeratotic plugs. The papillary layer of the corium was normal, and in the subpapillary layer and throughout the whole corium there were small and large well demarcated areas of cellular infiltration. The infiltrating cells were large, round or polygonal and undifferentiated and had a granular nucleus and little cytoplasm. Mitotic figures were numerous. In the large dense areas there was little stroma.

Treatment consisted of roentgen therapy and blood transfusions.

DISCUSSION

DR. E. W. NETHERTON: I think this condition is a rather rare type of leukemia. The nodules appeared while the patient was under observation. When they first appeared, they were almost purple, dark red or violaceous and much more infiltrated. Some roentgen therapy was given which accounts for the flattening of some of the lesions. My associates and I had one other case of this type of leukaemia cutis, but this is the only one that we have had an opportunity to follow for this long a period.

DR. C. L. CUMMER: What was the patient's complaint when he came under observation?

DR. E. W. NETHERTON: He complained of loss of weight and weakness. He had noticed before he came that his abdomen was enlarged, and he thought probably his spleen was enlarged.

CLAUDE BAZIL NORRIS, M.D., *President*

Oct. 28, 1937

C. L. CUMMER, M.D., *Secretary*

J. R. DRIVER, M.D., *Reporter*

Syphilis of the Central Nervous System with Thrombosis of the Anterior Choroid Artery. Presented by DR. W. F. SCHWARTZ (from the Department of Dermatology and Syphilology, the City Hospital).

S. B., a Turkish delicatessen owner aged 53, had been well until 9 p. m. on Oct. 14, 1937, when complete paralysis suddenly developed on the left side, with partial blindness in both eyes. When he was admitted to the City Hospital two days later, he was mentally clear and cooperative.

Examination showed complete anesthesia of the left side, with flaccid paralysis of the muscles on this side, including the left side of the face. There were left hemianopia of both eyes and auditory agnosia. Vital and gnostic sensations were absent on the left side. The blood pressure was 206 systolic and 106 diastolic. Examinations of the urine showed no albumin or sugar.

The Wassermann and the Kline test were strongly positive. The spinal fluid was clear, and the pressure was not increased. The Wassermann reaction of the spinal fluid was strongly positive in all dilutions, and a globulin test gave strongly positive results. The benzidine test gave negative results, and the mastic test showed a curve of 5555543210.

DISCUSSION

DR. W. F. SCHWARTZ: The question in this case is whether the condition is due to syphilis or to hypertension. The clinical diagnosis has been extremely precise, with typical findings. Consultation with the neurologist at the hospital produced the opinion that the etiologic factor in this case was probably syphilis rather than hypertension.

Foreign Body (Barberry) Dermatitis. Presented by Dr. W. F. Schwartz (from the Department of Dermatology and Syphilology, the City Hospital).

R. K., a man aged 33, states that a severe itching irritation developed on the hands, the arms, the thighs and the legs after he trimmed a barberry hedge one month ago. The eruption has been unusually persistent.

Over the arms, the forearms, the dorsa of the hands, the legs and the lower parts of the thighs there are many discrete papules and small nodules which show hyperpigmentation. The epidermis is intact over some, but many show small central ulcerations and pustulation. There are numerous scratch marks, and the tops of many of the lesions have been excoriated.

Biopsy of a nodule on the dorsum of the hand showed marked hyperkeratosis. In the subpapillary layer there was slight infiltration of lymphocytes. No giant cells or large mononuclear phagocytes were seen in the section.

DISCUSSION

Dr. J. R. Driver: The presence of tiny points of thorns may be responsible for the papular and almost nodular appearance of some of the lesions. The condition probably is a type of foreign body reaction to an irritating substance in a sensitized subject.

Dr. H. N. Cole: My associates and I have seen several patients who presented a similar dermatitis after working around a barberry hedge. I think this patient's condition would fall into the same group. The lesions on the thighs and the legs are produced by the pricks of thorns through the clothing.

Lichen Planus Sclerosus (Hallopeau, 1887). Presented by Dr. H. G. Miskjian.

J. L. M., a woman aged 34, states that lesions developed three years ago in a necklace-like arrangement at the base of the neck.

They consist of small flat whitish oval elements that have a peculiar porcelain hue. Their long diameter measures approximately 1 cm., and the individual elements are placed end to end, so that they give the impression of a string of beads arranged in two or three rows. Each small element is sharply defined; it is not raised above the surface of the skin; it has a shiny atrophic surface that looks like porcelain. Examination with a magnifier reveals white lines radiating from some of the elements toward the normal skin. There are, in addition, small horny dark brown or yellow plugs which are difficult to remove. They look somewhat like the seborrheic plugs of lupus erythematosus. In the middle of the back, close to the median line, there are two small round contiguous elements, which are slightly raised and have a central plug.

DISCUSSION

Dr. Emerson Gillespie, Canton, Ohio: I agree with the diagnosis. The lesions are slightly raised and whitish and are arranged in chain fashion.

Dr. H. G. Miskjian: I want to apologize for not presenting a biopsy report with this case, but I saw the patient for the first time today. Years after Hallopeau, in 1887, described the condition as lichen planus sclerosus, Darier described it under the name lichen albus.

Arsenical Eruption Precipitated by Carbarsone. Presented by Dr. Garrett Arthur Cooper (from the Department of Dermatology and Syphilology, the Lakeside Hospital).

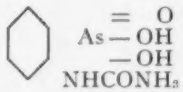
M. B., a woman aged 54, because of syphilis received during the past two years thirty injections of a bismuth compound and ten injections of mapharsen. In January 1937 a circumscribed area of dermatitis developed on the right thigh, and this exacerbated with subsequent injections of mapharsen. Administration of the arsenical was discontinued.

On Sept. 21, 1937, because of an infection with Trichomonas vaginalis the gynecologic department gave the patient carbarsone suppositories and 3¼ grain (0.24 Gm.) doses of the same preparation daily by mouth. After the first day the patient noted redness and burning of both hands and therefore discontinued the medication.

There is a diffuse, erythematous, scaling dermatitis of both forearms and hands. The palms show a reddish yellow cracking and scaling dermatitis, with some hyperkeratosis.

Serologic tests for syphilis gave strongly positive results.

The formula for carbarsone is as follows:



DISCUSSION

DR. H. N. COLE: I saw this patient yesterday and thought it would be interesting to show her, as the manufacturers of carbarsone emphasize its lack of toxicity. Emphasis should be laid on the fact that if a patient is sensitive to other arsenicals a physician may find difficulty, such as that shown by this patient, in using carbarsone.

Mycosis Fungoïde d'Emblée. Presented by DR. JOHN A. GAMMEL.

N. S., a healthy looking Italian boy aged 16, had had the usual diseases of childhood but no serious illnesses. Early in September 1937 he noticed a boil-like lesion on the flexor surface of the left forearm near the cubital fossa. This became larger and appeared flatter.

When the patient was first seen by me, on Oct. 9, 1937, the lesion was a flat, firm tumor about 4 cm. in diameter and 3 mm. thick. It had a somewhat pearly appearance, with numerous superficial new blood vessels. The central part was denuded but not ulcerated. The epitrochlear lymph node was of the size of a small cherry, and two soft lymph nodes were palpable in the left axilla. Examination of the skin and a general physical examination showed no further abnormality.

The Kahn and the Kline test were negative. The urine showed a slight trace of albumin but was otherwise normal. The erythrocyte count was 4,670,000, the leukocyte count 7,900, and the hemoglobin content 94 per cent. The differential blood count showed 71 per cent polymorphonuclears, 25 per cent lymphocytes, 2 per cent eosinophils and 2 per cent small mononuclears.

The histologic examination by Dr. Harry Goldblatt, of the Department of Pathology, Western Reserve University School of Medicine, showed a portion of the specimen to be denuded of epithelium. In the remainder of the specimen the epidermis was thick, and the rete and the papillae were well developed. Several layers at the surface of the epidermis were keratinized. In the remainder of the epidermis there was considerable vacuolation, and the cytoplasm of the epithelial cells was swollen. All through the epidermis, between the epithelial cells, there were a large number of polymorphonuclear leukocytes. The papillae were edematous and infiltrated with polymorphonuclear leukocytes, eosinophils and large mononuclear cells with a relatively large nucleus that stained uniformly. In the portion that was denuded of epithelium the entire corium was densely and diffusely infiltrated with polymorphonuclear leukocytes, both eosinophilic and neutrophilic, with mononuclear eosinophils, with some lymphocytes and with a large number of large mononuclear cells having oval, large violaceous nuclei. Plasma cells were present but were rare. Throughout the entire lesion there was a network of young capillary blood vessels. In some of these large mononuclear cells the nucleus had a horseshoe shape or a slight indentation on one side. Some of the large mononuclear cells suggested the myeloblastic series. In the deepest part of the section there was a focus of necrosis. A diagnosis of mycosis fungoides was suggested.

After doses of 100 roentgens on Oct. 16, 1937, and on Oct. 23, 1937, the lesion became flatter but ulcerated, with a dark red granular base.

DISCUSSION

DR. E. W. NETHERTON: The lesion has a clean central ulcer without an exudate and a glazed-over appearance with a thin crust. There is, in addition, a rather large node in the axilla. Histologically the lesion certainly has a polymorphonuclear type of infiltration. I should like to ask Dr. Gammel if it is customary in such cases to have such a definite regional adenopathy. I believe one would have to rule out other conditions—for instance, tularemia.

DR. JOHN A. GAMMEL: I cannot answer the question, but I shall have the patient tested for tularemia.

DR. H. G. MISKJIAN: I examined the biopsy section and agree with Dr. Goldblatt in his diagnosis of mycosis fungoides. After seeing the patient clinically, I can easily say that. I was somewhat puzzled, however, by the existence of a large number of cells that had nuclei homogeneously stained, and I could not classify them exactly. Dr. Gammel thought them of lymphocytic origin, and I think he is probably right. The histologic picture is against the diagnosis of tularemia. Clinically the disease does, I believe, resemble tularemia. I do not know about the regional adenopathy, but I should not see any objection to it in association with mycosis fungoides.

DR. E. W. NETHERTON: The only thing that confuses me is that there is such a distinct regional adenopathy. This unilateral large gland in the axilla seems to accompany this lesion early in its course. The condition might be an infection rather than mycosis fungoides. I suggested tularemia just as a type of infection. Can an absolute diagnosis be made from study of this biopsy specimen? I am trying to reconcile the regional adenopathy.

DR. H. G. MISKJIAN: On my own initiative I had no difficulty in reaching the conclusion that this condition was lymphoblastoma. On that basis I am accepting the diagnosis of mycosis fungoides.

A Case for Diagnosis (Granuloma Inguinale?). Presented by DR. C. G. LAROCCO.

L. M., a man aged 56, an Italian plasterer, states that about one year ago itching and burning developed about the glans penis and there was a painful swelling of the prepuce, associated with phimosis. He was circumcised in July 1937. Healing was slow, and in some areas ulceration developed.

The anterior third of the glans penis presents irregularly shaped ulcers extending to and involving the frenum. There is definite induration of this part of the glans, and the prepuce is indurated and produces a firm, constricting, cartilaginiform band when retracted. There are some superficial, irregular ulcers on the retracted prepuce.

The general physical examination showed no abnormality. Serologic tests for syphilis were negative, and smears showed no Donovan organisms.

A section from the prepuce showed the stratified squamous layer to be slightly thickened and the surface cells swollen. The epithelium formed a few thick projections into the dermis, but there was a well defined limiting membrane throughout. There were several areas just beneath the epidermis which showed spaces filled with pink-staining granular material. In the dermis there was an inflammatory lesion consisting of large masses of round cells, fibrin, some large wandering cells and an occasional large eosinophilic cell. There appeared to be some fibroblastic proliferation in the inflammatory areas. There were no giant cells, and no areas of necrosis were seen. A diagnosis of granulomatous cellulitis of the skin was made.

DISCUSSION

DR. H. N. COLE: I think this case is an example of xerosis balanitica. There is definite atrophy. Unfortunately, the microscopic picture does not corre-

spond, but the section was taken from the edge of the ulcer. I am not able to explain the ulceration, and the microscopic section showed no evidence of epithelioma. I thought that the process around the urethra showed a definite whitish, slightly depressed atrophy, such as one sees in kraurosis vulvae.

Metastatic Carcinoma in the Skin of the Neck. Presented by DR. GARRETT ARTHUR COOPER (from the Department of Dermatology and Syphilology, the Lakeside Hospital).

J. F., a man aged 44, a steel worker, on July 15, 1937, was struck on the right side of the vertex of the head while at work. Examination at that time revealed no lesions. However, on Aug. 20, 1937, a lesion which was proved by histologic examination to be squamous cell carcinoma was incompletely removed from this area of the scalp. On Sept. 3, 1937, the entire area was excised. Shortly thereafter the patient noticed a small lesion on the right side of the neck. This has enlarged.

The lesion, approximately 2 cm. in diameter, is slightly raised and moderately infiltrated, appears to be noninflammatory and is movable over the subcutaneous structures. No adenopathy is demonstrable.

General physical examination showed no abnormality and there was no other evidence of cancer.

The section taken for biopsy showed stratified squamous epithelium, hair follicles and sweat and sebaceous glands. The epidermis was intact and not invaded. Scattered through the corium and the subcutaneous tissues were numerous tumor masses lying in apparently preformed spaces which were thought to be lymphatic vessels. At one edge there was an invasion into the subcutaneous tissue. The tumor masses were composed of squamous epithelium which showed pavement architecture in most places. There were few areas of keratohyalin but no pearl formation. There were extreme pleomorphism and many mitotic figures.

DISCUSSION

DR. JOHN A. GAMMEL: I saw this man three weeks ago, and at that time the lesion on the neck was soft and clinically resembled lymphoid tissue. I thought of lymphangioma as the probable diagnosis and was greatly surprised when the biopsy revealed carcinoma.

DR. H. N. COLE: This case illustrates the necessity for histologic examination in any debatable dermatologic condition. Clinically I could not have made the correct diagnosis.

DR. J. R. DRIVER: This type of tumor must be most unusual. I have never before seen a metastasis in the skin so far removed from the primary lesion without involvement of the lymph nodes.

DR. GARRETT ARTHUR COOPER: I was interested in the rapid appearance of this lesion after the excision of the one on the scalp, without any evidence of lymphatic extension. It makes one wonder whether it is metastatic.

DR. G. W. BINKLEY: The section shows large atypical cells. There were no prickle cells, but it is not necessary to have them to be sure of a diagnosis of prickle cell carcinoma. I thought the section was a beautiful one for secondary squamous cell carcinoma of the skin. The epidermis was not involved in any portion of this growth.

DR. H. G. MISKJIAN: I studied the slide and had difficulty in calling the condition squamous cell epithelioma. There is no question but what the process is malignant, but the cells in the section were not prickle cells and were more or less undifferentiated. One would not have difficulty in attaching them to any structure in the normal skin if one saw them independently. I should prefer to leave out the word "squamous" and call the condition carcinoma. It is probably more malignant than is suspected.

A Case for Diagnosis (Atopic Dermatitis? Lupus Erythematosus?). Presented by DR. EDWARD STEINBERG.

C. M. S., a healthy-appearing man aged 72, states that his trouble began about one year ago with a spot the size of a small coin on his scalp; this had a weeping, red, denuded surface. In the following weeks similar lesions developed on the scalp and on the face. The disease has slowly progressed, until at the present time there are numerous lesions on the scalp, the face and the upper portion of the chest.

The lesions are rather sharply defined, varying from a few millimeters to about 2 cm. in diameter. Some show denuded, red, weeping surfaces, while others are dry, with greasy scales on the surface. There are no bullous lesions, and no involvement of the mucous membranes of the mouth has been noted.

The eruption has resisted various types of topical applications and several roentgen treatments. There is no history of ingestion of drugs.

General physical examination showed no abnormality. Serologic tests for syphilis gave negative results.

A biopsy specimen was not obtained.

DISCUSSION

DR. R. E. BARNEY: I think this man's eruption has some features of the Senear-Usher type of pemphigus. The lesion on the face looks like lupus erythematosus. I think the prognosis is unfavorable.

DR. J. EDGAR FISHER: To me the eruption looks like pemphigus with lesions resembling lupus erythematosus. I previously saw a patient with a condition similar to this, but the prognosis was favorable, and the man is still alive. If this condition is pemphigus, it is a mild form of that disease.

DR. H. J. PARKHURST, Toledo, Ohio: I wonder whether this might not be a bullous type of lupus erythematosus, especially since the mucosa of the mouth has not been involved thus far.

DR. E. W. NETHERTON: I feel that this is a Senear-Usher type of pemphigus. If it were a disseminated type of lupus erythematosus, constitutional symptoms would probably be present.

DR. CLAUDE BAZIL NORRIS, Youngstown, Ohio: I should like to ask the members if they believe Nikolsky's sign is specific in the diagnosis of pemphigus.

DR. H. N. COLE: If Nikolsky's sign is present, it means a great deal, but its absence does not always mean much. The fact that the problem is to differentiate between lupus erythematosus and pemphigus makes me think that the condition is the Senear-Usher syndrome. Some patients with this condition live for a long time.

SAN FRANCISCO DERMATOLOGICAL SOCIETY

N. N. EPSTEIN, M.D., *President*

Oct. 1, 1937

H. V. ALLINGTON, M.D., *Secretary*

Condyloma Acuminatum. Presented by DR. H. J. TEMPLETON, Oakland, Calif.

D. B., a white woman aged 22, first noted growths on her vulva after the birth of her child, two months ago. Inspection reveals confluent verrucous masses involving both labia, the perineum and the perianal area. They measure approximately 2½ inches (6.4 cm.) in depth and 6 inches (15 cm.) anteroposteriorly. The Wassermann reaction was negative.

DISCUSSION

DR. MERLIN TREVOR-ROPER MAYNARD, San Jose, Calif.: Does Dr. Templeton consider this condition a syphilitic or a nonsyphilitic condyloma?

DR. A. E. INGELS: I recall the case of a syphilitic Negress who was seen in the clinic because of extensive condylomas involving the labia and the anal opening. Antisyphilitic treatment alone was started but was not effective. Electrocoagulation was then added gradually, and this gave results that I did not believe were possible.

DR. HARRY E. ALDERSON: I did not see the patient presented tonight. I should like to ask Dr. Ingels if the lesion was too extensive for use of the butane spray to be feasible.

DR. A. E. INGELS: I should not think so.

DR. H. J. TEMPLETON, Oakland, Calif.: The involvement in this case is the second most extensive that I have seen in a case of condyloma acuminatum. I believe that it is not due to syphilis. I have previously had satisfactory results from treatment of conditions similar to this, although not so extensive, by electrocoagulation. Thus far no treatment has been given in this case except five weekly injections of distilled water and local application of boric acid powder. With this treatment the masses have retrogressed, I believe, about 30 per cent. I shall continue this therapy purely experimentally, but I believe that eventually the remainder of the masses will have to be removed by actual cautery or electrosurgical treatment.

Keratoses of the Face. Presented by DR. H. J. TEMPLETON, Oakland, Calif.

Mr. J. T., aged 74, is presented for suggestions as to therapy of inveterate generalized keratoses of the face which go on to malignant degeneration.

I have been watching Mr. T. since 1934, during which time I have removed four definite epitheliomas, as well as many borderline keratoses, from various parts of his face. I have attempted to control the tendency to the formation of keratoses with ointments containing sulfur and salicylic acid and with solid carbon dioxide. Treatment of one small area with beta rays of radium was beneficial. However, I was afraid to continue this because of a history of an unknown amount of previous roentgen treatment to the face.

DISCUSSION

DR. O. P. DIEDERICH, Fresno, Calif.: This condition is frequently seen in the San Joaquin Valley, due to excessive sunlight. I usually recommend the use of an electric shaver to lessen the cutaneous irritation.

DR. L. R. TAUSSIG: A patient of this sort is sensitive to sunlight. A part of the treatment should be to protect him from the sun as much as possible. There are preparations on the market containing methyl salicylate which at least partially filter out the harmful rays of the sun.

One is tempted to use radiation on a patient of this sort. I think that is definitely contraindicated. I am certain that it should not be applied to any large portion of the face. The patient should be warned to keep in fairly close touch with his dermatologist because of the likelihood of further malignant degeneration.

DR. HARRY E. ALDERSON: I think the things to do here are to apply the most soothing, softening preparation possible and to protect the skin against the sun. Nothing containing salicylic acid should be applied because of its stimulating effect on the entire epidermis, the basal layer particularly. The patient is 74 years old, and epitheliomas in older persons are not as malignant as they are in younger persons. Any lesion that appears to be a menace can be destroyed by electrocoagulation.

A Case for Diagnosis (Lupus Erythematosus? Psoriasis?). Presented by Dr. H. J. Templeton, Oakland, Calif.

Mrs. M. C., a white woman aged 55, was referred by Dr. George Calvin, of Oakland, Calif., who supplied the following history and physical data: About four months ago a dull red, scaly rash appeared over the bridge of the nose. It gradually spread over the nose and the adjacent portions of the cheeks and developed on the rims of the ears, the upper anterior portion of the chest, the elbows, the forearms, the knees and the legs. The patient was badly bruised and shaken in a fall ten years ago and has not been in robust health since. She is said to have had an attack of psoriasis eight years ago, which cleared after a few weeks. Her weight has decreased over the last eight or ten years from 130 to 85 pounds (59 to 38.5 Kg.), 15 pounds (6.8 Kg.) being lost in the past year. She underwent hemorrhoidectomy in 1925. Her menses stopped in 1935. In the past year or two she has complained of intermittent pain and soreness in the left shoulder and the right side of the hypochondriac area, fatigue, numbness and coldness of the extremities and abdominal gas. She believes her eruption began at a period when she was doing some painting in renovating her apartment and thinks it has improved some since this was stopped three weeks ago. Physical examination revealed a small (59 inch [150 cm.] tall) woman, who was poorly nourished and, while not acutely ill, was weak almost to the point of exhaustion. Her tonsils showed evidences of chronic infection, and she had a polyp of the uterine cervix. A blood count revealed 77 per cent hemoglobin, 4,020,000 erythrocytes and 12,000 leukocytes. The differential blood count showed 65 per cent polymorphonuclears, 28 per cent small monocytes, 6 per cent large monocytes and 1 per cent eosinophils. The blood platelet count was 60,000. Urinalysis showed no abnormality. The basal metabolic rate was —5 per cent.

I first saw the patient a month ago. The lesions over the face, the ears and the upper part of the chest exhibited a dull reddish color, infiltration, hyperkeratosis and follicular plugging strongly suggestive of lupus erythematosus. Those on the extremities, however, were discrete and less infiltrated, showed fine silvery scaling and looked less like lupus erythematosus than psoriasis. The patient looks and feels generally much better at present. For the past month she has been in bed on a high caloric diet, including a quart of milk a day. She has taken iron, capsules containing vitamins A, B and D and from ½ to 1 grain (0.03 to 0.06 Gm.) of thyroid daily. An ointment of zinc oxide has been applied to the eruption.

DISCUSSION

Dr. N. N. Epstein: I think that the diagnosis in this particular case will rest on the pathologic observations. Certainly from a clinical standpoint psoriasis is present, and whether the lesions on the face are psoriasis or lupus erythematosus will have to be determined by the clinical course and the pathologic picture.

Dr. L. R. Taussig: Psoriasis of the face may resemble lupus erythematosus.

Dr. Harry E. Alderson: It is interesting to see two different conditions in a patient, one of which is the result of solar sensitiveness and the other one that ordinarily responds to sunlight or treatment with a quartz lamp. I believe that the lesions on the elbows are definitely psoriasis. The involvement of the area on the chest certainly demonstrates that the woman is sensitive to sunlight.

Dr. C. J. Lunsford, Oakland, Calif: The patient says that she did not have a sunburn at the onset and has not been frequently exposed to sunlight.

Dr. Merlin Trevor-Roper Maynard, San Jose, Calif.: I have had two patients with psoriasis who presented lesions on the face and the neck as well as on the covered portions of the body. Treatment of both with autohemotherapy caused clearing of the lesions from the body but had no effect on those on the face and the neck.

Dr. H. J. Templeton, Oakland, Calif.: I have felt that this condition was a combination of two diseases, lupus erythematosus and psoriasis, and it inter-

ested me to find that the patient had an extremely depressed thrombocyte count, 60,000. In a number of cases of lupus erythematosus low platelet counts have been found.

Hyperhydrosis of the Buttocks. Presented by DR. H. J. TEMPLETON, Oakland, Calif.

R. M. J., a man aged 22 years, complains of attacks of perspiration of the buttocks so severe as to wet the seat of his trousers when he sits on a chair. These become worse when he is nervous or when he has trouble with the lower part of the bowel, such as constipation, diarrhea or fissures, which trouble him occasionally.

A complete physical examination by Dr. C. J. Burnham, of Berkeley, Calif., showed no essential abnormality. A 15 per cent solution of aluminum chloride has been of slight help.

DISCUSSION

DR. HARRY E. ALDERSON: I think that sponging that area for four or five days with dilute solution of formaldehyde, followed by dusting with methylene ditannin powder, would give the patient relief for a short time anyway. Even if the treatment does dry the skin too much or cause irritation, it will greatly slow down the secretion of the sweat glands.

DR. H. J. TEMPLETON, Oakland, Calif.: This man is greatly distressed by his problem. I think that the condition is on a functional basis and not due to any organic disease. I asked a neurosurgeon whether something could be done neurosurgically, but when he figured out that he would have to section the sympathetic nerves around the abdominal aorta, he did not want to do it. Dr. Allington pointed out that there may be a conflict in this patient's mind because of contemplated matrimony.

Tularemia. Presented by DR. ORLAND F. MONTGOMERY.

M. L. B., a white man aged 42, states that while he was skinning and dressing wild rabbits near Jackson, Amador County, Calif., between September 4 and 6, he noticed three abrasions on the right hand. He had generalized chills on September 7 and 8. On September 10, when he was first seen, he was mildly ill and pale. The temperature was 98.6 F.

He now shows three small ragged punched-out ulcers on the right palm and the fingers. There is lymphangitis of his right forearm, with a suggestion of a "rosary-like" nodular infiltration along the course of the lymphatic vessels. A moderately hard swelling of the right epitrochlear and axillary lymph nodes is present, and there is an extraordinarily acute and dark red conjunctivitis of the right eye (without purulent discharge). The lymph nodes over the right parotid region are swollen, hard and tender. Agglutination tests done at the Hooper Foundation gave positive indications of tularemia with dilutions up to 1:160. They showed no sign of Malta fever or of typhoid fever.

DISCUSSION

(All members agreed with the diagnosis.)

Lupus Erythematosus Treated with Sulfanilamide. Presented by DR. A. E. INGELS.

CASE 1.—Mr. J. B. McG. is a well nourished, well developed man, aged 50, who appears well.

The patient entered the dermatologic clinic of Stanford University Hospital on July 13, 1937. At that time he showed widely disseminated lesions on the face and the backs of the hands of four months' duration. Since the time the lesions first appeared they had been enlarging continuously. He had had no treatment. He noticed that exposure to the sun aggravated the eruption.

The patient had an attack of urethritis thirty-five years ago. He states that he has not had syphilis. He had lead poisoning, colic and neuritis two years ago. No internal medication was given.

A general examination showed nothing of importance except many carious teeth.

Roentgenograms of the chest showed clear pulmonary fields, with ordinary markings peribronchially and around the roots of the lungs. A tuberculin test with a dilution of 1:10,000 gave negative results. The blood and the urine were normal. The Wassermann reaction was negative and had been negative two and one-half months and two years ago. Microscopic study showed typical lupus erythematosus.

On July 21 treatment with sulfanilamide in a dose of 0.6 Gm. three times a day was begun. The lesions paled at first. Ten days after the beginning of treatment the patient felt ill. The administration of sulfanilamide was discontinued at this time. The lesions were then slightly worse. An acute flare-up occurred after another week. Medication was resumed on August 12 in the same dosage. On the next day all the lesions reacted with an angry red flare-up. At this time generalized dermatitis medicamentosa developed. This was distributed evenly over the entire body and resembled syphilitic roseola. However, the patient's general condition was good. The administration of sulfanilamide was discontinued.

On August 20 the face and the hands looked better than at any time before. On September 20 both the face and the hands had completely cleared; the patient's general condition was good.

A photograph of the patient taken before treatment is presented. Sections are presented for microscopic study.

Case 2.—Miss M. R., a white woman aged 45 years, is presented for Dr. Alderson.

She entered the office an April 16, 1937, at which time she had had lupus erythematosus on the face for eight months. The lesions were localized on the right and the left side of the forehead and both sides of the bridge of the nose and were acutely infiltrated. One scar on the bridge of the nose was suggestive of healed lupus erythematosus; however, the patient blamed this on an injury. She stated that the sun always irritated her skin. Her general condition was good except that she was overweight. She never had had any pulmonary trouble. The Wassermann and the tuberculin test gave negative results.

She was treated with local applications from April 16 to May 27. From May 27 to July 15, 1937, she received weekly injections of bismuth subsalicylate, which produced no change in the lesions. Therefore, administration of sulfanilamide in a dose of 0.6 Gm. three times a day was started on July 15 and continued until July 31. She reacted with hot flushes but showed decided improvement. Medication was resumed on August 8 and continued until August 25, at which time the face had cleared entirely. The patient had flushes at this time. The temperature remained normal. The white blood cell count decreased from 7,350 to 6,900. Otherwise, there were no toxic symptoms.

On September 10 eczematous patches were observed on both elbows; the patient believed that she had had these for some time. Local treatment to these for ten days produced improvement.

Case 3.—Mr. D. T. L., a white man aged 25, entered the dermatologic clinic of Stanford University Hospital on Feb. 9, 1937, for treatment of lupus erythematous.

The lesions had started five years before, on the upper and the lower parts of the cheek, the forehead, the nose, the upper part of the left arm, the ears and the scalp. Some of the lesions had persisted since then; some had healed with scarring. The patient had always been sensitive to sunlight.

Local treatment had been ineffective. Twenty-five intravenous injections of a gold preparation in three or four years had effected some improvement, but the condition again had become worse. The last injection had been given in April

1936. Twenty injections of a bismuth preparation had been given intramuscularly, the last one on Dec. 1, 1936. He had had no treatment since that date.

When he came under observation on Feb. 9, 1937, the lesions were most pronounced on the cheeks. Almost the entire face was covered. The lips were red, ulcerated, swollen and extremely tender. There was a lesion on the left side of the hard palate, which extended onto the alveolar process.

Microscopic study of tissue from the face showed lupus erythematosus with atrophy. The Wassermann reaction was negative. A blood count on Feb. 10, 1937, showed 4,890,000 erythrocytes. The differential count showed 47 per cent polymorphonuclear neutrophils, 44 per cent lymphocytes, 4 per cent monocytes and 5 per cent eosinophils. Tuberculin tests on two occasions gave negative results.

Oral treatment with from 1 to 2 Gm. of sodium bismuthate daily was started, and some improvement was noted during February and March. The lesions resumed their old appearance about May 1. Seven weekly injections of 20 mg. of sodium gold thiosulfate were given intravenously, beginning May 14, 1937. No obvious change resulted.

The administration of sulfanilamide in a dose of 0.6 Gm. four times daily was started on July 2 and continued for fourteen days. The left side of the face and the lips improved quickly. However, a drug reaction similar to a phenobarbital rash or a syphilitic roseola appeared. This covered the entire body and was accompanied with moderate itching. The patient complained of sore throat, general malaise and some nausea. The medication was discontinued, and the drug rash cleared in a few days. The lips healed quickly, and the eruption on the left side of the face showed no activity, while that on the right side showed only slight activity. On August 2 administration of sulfanilamide was again started, with a dose of 0.3 Gm. four times a day. After two days an acute flare-up of all the lesions of lupus erythematosus occurred. Treatment with sulfanilamide was then discontinued. On August 13 the lesions again began to clear without further treatment, and the left side of the face and the lips healed entirely, showing no redness. On August 25 the patient felt well. On September 4 there was a flare-up of the lesions on the right side of the face and the lips, and there was some activity on the left side of the face as well.

Although the face is about 50 per cent better than it was when treatment with sulfanilamide was started, the result still leaves much to be desired.

A photograph taken before treatment and microscopic sections are presented.

CASE 4.—Mr. W. C., a white man aged 42, entered the dermatologic clinic of Stanford University Hospital on Feb. 25, 1937, for treatment of lupus erythematosus of two and one-half years' standing.

At the time of entry he showed extensive lupus erythematosus of the nose and the cheeks, with pronounced scarring in the center and activity in the periphery. The lesion on the left cheek was particularly active. The lupus erythematosus had started after overexposure to the sun and had persisted since then, with flare-ups and remissions. The patient had had four roentgen treatments in 1936, and a flare-up had occurred after each treatment. No intravenous or oral treatment had been given.

On entry, a diagnosis of rheumatic cardiac disease was made in the medical clinic, and administration of digitalis was started on March 29. The patient had chronic sinusitis.

The blood count showed 4,710,000 erythrocytes, 87 per cent hemoglobin and 6,100 leukocytes. The differential count showed 63 per cent polymorphonuclear neutrophils, 2 per cent eosinophils, 34 per cent lymphocytes and 1 per cent monocytes.

The Wassermann reaction was negative. The tuberculin test with a dilution of 1:10,000 gave negative results. Roentgen examination of the chest showed no abnormality.

The patient was given sodium bismuthate, 4 Gm. three times a day, and nausea and bismuth stomatitis followed. At first there was no change in the lesions,

but on April 9 they appeared to be worse. He was then given intravenous injections of from 10 to 30 mg. of sodium gold thiosulfate. This caused nervousness and loss of appetite. The urine and the blood at this time were normal. The lesions remained unchanged until July 8, when an acute flare-up was noted.

Administration of sulfanilamide, in a dose of 0.6 Gm. four times a day, was started on July 9. His condition improved quickly, and all the lesions paled. However, when seen on July 20, he had anorexia, "feverishness" and an exacerbation of his lesions. His temperature was found to be normal. Treatment with sulfanilamide was discontinued. By July 27 the lesions had improved about 50 per cent. On August 3 the cheeks were clear except for an active lesion, about 2 by 1 cm., on each side of the face, at the lower part of the original lesion. Sulfanilamide therapy was resumed on August 5 and discontinued on August 9, because of nausea, malaise and a temperature of 37.3 C. (99.14 F.). The lesions continued to clear. Treatment with sulfanilamide, in a dose of 0.3 Gm. four times a day, was resumed on August 16, but the symptoms of intolerance returned the next day and it was discontinued.

By August 20 the skin had begun to improve. Nevertheless, the patient still did not feel well and salivated a good deal. At this time he was given yeast tablets, which produced some benefit.

On September 24 the skin was almost clear. It was thought that his continued lassitude and mild general malaise might be partially due to malnutrition, as he was living on a markedly limited budget. His blood count on this date showed 5,020,000 erythrocytes, 90 per cent hemoglobin and 5,000 leukocytes. The differential count showed 74 per cent polymorphonuclear leukocytes, 22 per cent lymphocytes and 4 per cent monocytes.

Photographs taken before treatment and microscopic sections are presented.

CASE 5.—L. W., a Chinese girl aged 16, entered the dermatologic clinic of Stanford University Hospital on May 23, 1936, for treatment of lupus erythematosus of four years' duration. The lesions were confined mainly to the areas below and lateral to the left eye and involved the lower left eyelid, including the margin of the mucous membrane. The lesions were red, inflamed and active. When the condition started with a pimple, four years ago, ultraviolet radiation was given weekly for one year. The lesions became more extensive and angry in appearance. Treatment for nine months with sodium gold thiosulfate, both intradermally and intravenously, produced some improvement. Twelve intramuscular injections of a bismuth preparation followed this, the last one having been given in December 1935. Treatment with solid carbon dioxide was tried for two weeks, but this produced no change. For three months before coming under my observation the patient had received ultraviolet radiation without effect.

There was no family history of tuberculosis. The patient had swollen glands in the neck at the age of 7 years.

Roentgenograms of the chest on June 23 showed infiltration around the root of the right lung which was suggestive of tuberculosis—evidently not a recent process. The Wassermann reaction was negative. The blood count on June 25, 1937, showed 4,820,000 erythrocytes, 85 per cent hemoglobin and 10,200 leukocytes, and the differential count showed 42 per cent polymorphonuclear neutrophils, 2 per cent eosinophils, 54 per cent lymphocytes and 2 per cent monocytes.

Bismuth subsalicylate was given weekly beginning June 28, 1936, until Jan. 12, 1937, but produced no improvement. Roentgenograms of the chest at this time showed no further change. On Feb. 8, 1937, administration of sodium gold thiosulfate, in weekly injections of from 10 to 15 mg., was started; this was discontinued on July 28, 1937. Some improvement resulted. During this time cervical lymphadenopathy developed.

Treatment with sulfanilamide, in a dose of 0.3 Gm. four times daily, was started on July 28. It was given for fourteen days and resulted in appreciable improvement. No untoward symptoms developed. After a twelve day interval medication was resumed. The patient's condition continued to improve. During this time conjunctivitis developed in the left eye. After eleven days the medica-

tion was again discontinued. It was resumed on September 15. The lesions continued to improve until September 24, when the conjunctivitis recurred and the administration of sulfanilamide was discontinued. Examination in the ophthalmologic clinic on both occasions showed nothing abnormal to account for the conjunctivitis, which was mild.

Since the giving of sulfanilamide has been discontinued, the lesions have continued to improve.

A blood count on Sept. 29, 1937, showed 4,400,000 erythrocytes, 79 per cent hemoglobin, 71 per cent polymorphonuclear neutrophils, 1 per cent eosinophils, 26 per cent lymphocytes and 2 per cent monocytes. The red blood cells showed rare poikilocytosis and occasional anisocytosis.

Microscopic sections are shown. The photograph of the lesion presented was taken five days ago.

DISCUSSION

DR. HARRY E. ALDERSON: Dr. Ingels' results with these patients have been interesting and striking. It is known that in a good many cases lupus erythematosus is associated with streptococcic foci. That is the reason for this form of therapy.

DR. N. N. EPSTEIN: Sulfanilamide has taken practitioners by storm. The toxic effects of the drug are not yet sufficiently well known. At the University of California Hospital hepatitis developed in 1 case, and in the clinic general cutaneous eruptions appeared in 2 cases, after the use of sulfanilamide. In cases in which gonorrhea was treated with sulfanilamide many recurrences are being observed. The drug has not proved effective in the treatment of many streptococcic infections, such as scarlet fever, endocarditis and bacteremia. It seems to me that to gage the effects of the drug on such conditions at this time would be premature. The drug should be used judiciously and only in selected cases, as in Dr. Ingels' series; it should not as yet be recommended for general use in the treatment of lupus erythematosus.

DR. H. J. TEMPLETON, Oakland, Calif.: Without wishing to detract a bit from Dr. Ingels' results, I am wondering whether a drug which is known to hammer down the leukocyte count is indicated in the treatment of a disease that is frequently accompanied with leukopenia.

DR. L. R. TAUSSIG: Sulfanilamide is evidently going to be widely used in practice. The drug is certainly toxic and may have late effects of which nothing is known. The toxic effects so far observed seem to stop when administration of the drug is withdrawn.

Patients with lupus erythematosus are definitely sensitive to light. A recent article (Frank, L. J.: Dermatitis from Sulfanilamide, *J. A. M. A.* **109**:1011 [Sept. 25] 1937) pointed out the fact that one of the untoward effects of sulfanilamide is the production of sensitization to sunlight. This is a contraindication for its use in lupus erythematosus. Lupus erythematosus may be due to foci of streptococcic infection, and this fact may justify its trial under carefully controlled conditions.

The cases presented tonight were not sufficiently convincing to arouse enthusiasm for this method of treatment.

DR. A. E. INGELS: Groping for an effective remedy for the treatment of lupus erythematosus, I thought the theory that focal infection was its source might suggest the use of sulfanilamide.

In all the 5 cases in which this treatment was used there was improvement. In 2 cases there was complete clearing. The patient in case 3 was almost well but had an acute flare-up a few days ago. However, he is still 50 per cent better than when medication was started.

The tuberculin test gave negative results in cases 1, 3 and 4. The patient in case 2 stated that she had never had thoracic symptoms. Roentgenograms of the chest were suggestive of healed pulmonary tuberculosis in case 5 (that of the Chinese girl). In the other cases the roentgenograms showed no abnormality. None were taken in case 7.

Sulfanilamide was given four times daily in a dose of 0.6 Gm. in the first 4 cases and of 0.3 Gm. in case 5. It was never given for more than fourteen days at a time. All but 1 of the patients showed reactions in one form or other. Two had generalized dermatitis medicamentosa, and 2 suffered from fatigue, hot flushes and nausea. The fifth, the Chinese girl, had shown no untoward symptoms except conjunctivitis. She has had approximately thirty-three days of medication.

The blood count showed no marked changes in any case except the fifth, in which there were slight anisocytosis and poikilocytosis. Repeated examination showed no untoward changes in the differential count.

In 2 cases (3 and 5) mild indifferent applications were given.

Two other cases in which treatment has not yet started will be reported later.

Lupus Erythematosus Involving the Eyelids. Presented by DR. C. J. LUNSFORD, Oakland, Calif. (from the E. O. Cowell Memorial Hospital, Berkeley, Calif.).

A. B., a white man aged 21, states that his eruption began in the spring of 1935 on the vermilion border of the right side of his lower lip. Within the next several months first the left and then the right lower eyelid became involved, and a small area developed on the left arm over the insertion of the deltoid muscle. In March 1937 a lesion appeared on the bridge of the nose; and in April, after local injury, one on the left side of the vermilion border of the lower lip. These are typical of discoid lupus erythematosus. They are moderately infiltrated and have slowly spread peripherally, leaving noticeable central atrophy. At present the lesions on the eyelids are roughly crescent shaped, involve the free margins of the lids and include the upper third of the cutaneous surface of the lids. There is a partial loss of the eyelashes. The other lesions are roughly from 1 to 2 cm. in diameter. No treatment has been of permanent benefit.

The case is presented because of the unusual picture of lupus erythematosus of the eyelids.

DISCUSSION

DR. STUART C. WAY: I believe that involvement of the eyelids in this disease is more common than is generally realized. Ophthalmologists frequently mention seeing lupus erythematosus of the lids.

A Case for Diagnosis (Erythema Elevatum Diutinum, Plus Erythematous Eruption of the Face?). Presented by DR. H. V. ALLINGTON.

This patient, an Italian boy aged 6½ years, was first seen in consultation with Dr. E. R. Guinan of Richmond, Calif., on Sept. 18, 1937. About six months ago several small, nontender papules were noted on the dorsa of the knuckles and the interphalangeal joints of the fingers. These have increased in size and number and coalesced to form small plaques. Subsequently a few developed on the extensor surfaces of the elbows.

About six weeks ago a mild erythematous scaling dermatitis appeared on the face; this was noted to be aggravated by exposure to sunlight. The patient otherwise has been healthy and active. Dr. Guinan reported a careful physical examination to show nothing relevant.

The patient is a fair-haired blond. The lesions on the fingers in some areas cover the whole dorsal surfaces of the joints. They are not reddened; some are slightly paler than the normal skin. They are flat topped, and their surfaces are slightly irregular, indicating the outlines of the individual lesions from which they developed. Some of them show a shallow central depression filled with an adherent thin horny scale. They are firm and freely movable over the subcutaneous tissues.

The eruption on the cheeks consists of mild erythema and superficial scaling, resulting in an irregular decrease in pigmentation. It affects the areas of the

nose, the forehead and the cheeks most exposed to sunlight. There is no definite infiltration, telangiectasis, follicular hyperkeratosis or atrophy.

Sections from a lesion on a finger are shown. These revealed a moderate degree of hyperkeratosis and acanthosis, with some flattening of the rete pegs. There was an increase in the granular layer of the epidermis. Some edema and basophilic degeneration were present in the papillae and the subpapillary area, and a perivascular cellular infiltrate was most marked in these areas. The process was intense enough in some places to have caused disorganization of the basal layer and small areas of hyaline degeneration immediately beneath the epidermis. The deeper layers of the cutis showed increased fibrosis and a moderate perivascular infiltrate. The inflammatory cells were chiefly lymphocytes with a few epithelioid cells and an occasional plasma cell. There was no definite tubercle formation.

The Wassermann test and examination of the urine showed no abnormalities. Tuberculin tests (with old tuberculin in dilutions of 1 : 1,000 and 1 : 100) gave negative results.

DISCUSSION

DR. HARRY E. ALDERSON: I saw a woman recently who had so many warts on the back of her finger that one could hardly count them. They resembled closely those seen on this patient, whom I saw hurriedly as he was leaving. I am perfectly willing, however, to accept Dr. Allington's diagnosis.

DR. G. V. KULCHAR: I think that this case is one of erythema elevatum diutinum. I want to know whether the child has ever had rheumatic fever. The distribution on the hand is typical. I do not believe the lesions are warts.

DR. STUART C. WAY: The lesions on the elbows superficially resemble xanthoma.

DR. H. V. ALLINGTON: There is no history of rheumatic fever in this patient. It is interesting to consider the possibility that these lesions are tuberculids. The eruption on his cheeks might suggest early, mild lupus erythematosus.

A Case for Diagnosis (Erythematous Nodules of the Face and the Back?).
Presented by DR. N. N. EPSTEIN and Dr. E. A. LEVIN.

A. B., a white man aged 52, is a watchmaker. An eruption began eight years ago as erythematous nodules on the face, the neck and the back. These persisted without symptoms for weeks or months and then disappeared. They have varied in size up to that of a dollar. There is at present a group on the center of the back and several on the face.

The blood count and the urinalysis showed no abnormality. A section is presented.

The patient was fully investigated by Dr. Templeton several years ago.

DISCUSSION

DR. H. J. TEMPLETON, Oakland, Calif.: I saw this patient on Feb. 15, 1933, because of a circinate group of papules the size of a 25 cent piece on the right cheek, which had begun two years before. A palm-sized group of similar slightly indurated papules on the right breast and a smaller group over the ninth dorsal vertebra had come during the previous ten days. There had been no recent illnesses, and there was no history of the ingestion of drugs. The appearance of the lesions suggested secondary syphilis. The Kline, the Kahn and the Wassermann test of the blood were negative. A biopsy performed on Feb. 17, 1933, showed a marked perivascular round cell infiltrate.

The patient received 5 doses of ¼ skin unit of roentgen radiation between February 28 and March 27, 1933. The only other treatment was the administration of calcium lactate by mouth. He was not seen from March 27 until Dec. 21, 1933. At that time the lesions were still present over the right breast.

He was next seen on Feb. 13, 1934, when a cutaneous test for syphilis was done. The result of this was inconclusive, however, because of a severe reaction in both the test site and the control. His skin was practically well at that time, and he did not return for further observation.

DR. N. N. EPSTEIN: If the lesions were limited to his face, I should think the condition was lupus erythematosus. The group of erythematous nodules on the back came in the same place Dr. Templeton described. The condition is most likely a fixed erythema.

A Case for Diagnosis (Leprosy?). Presented by DR. STUART C. WAY.

J. B., a man aged 62, a native of Mexico, was first seen at the dermatologic clinic of the Mary's Help Hospital on Aug. 26, 1937. The initial lesion had appeared four months before, on the left forearm, in the form of a small papule which itched intensely and enlarged rapidly. Several weeks before his entry, new lesions, dusky red, sharply circumscribed and moderately indurated, developed on the neck, the right arm, the chest, the legs and the lobes of the ears. A few of the lesions were covered with fine scales and resembled the manifestations of a mycotic infection.

The patient stated that, with the exception of his eruption, he had been in excellent physical condition. A neurologic examination by Dr. E. F. Stadtherr showed that the affected parts were completely anesthetic. The ulnar nerves did not appear to be enlarged.

The blood count and urinalysis showed no abnormality. The Wassermann and the Kahn test were negative.

Scales removed from a lesion on the right arm when planted on Sabouraud's medium produced a luxuriant growth within seven days. The fungus has not been classified.

Microscopic examination of tissue removed from the right and the left arm when stained by the Ziehl-Neelsen method failed to show an acid-fast bacillus.

DISCUSSION

DR. OSTWALD: This case is interesting because the lesion and the symptoms seem to be those of lepra even though no lepra bacilli were found. I had a similar case some years ago, in which the lepra bacilli could not be found at first in the tissue but later were found in material from the nose and the throat. Subsequently a biopsy specimen from the border of the lesion showed lepra bacilli.

DR. STUART C. WAY: Nasal smears showed no bacilli in this case.

NOTE.—This patient was referred to the Department of Public Health because of the clinical diagnosis. Lepra bacilli were afterward found.

Neural-Leprosy. Presented by DR. F. G. NOVY JR., Oakland, Calif.

F. J., a man aged 31, was born in Hawaii and lived there until he was 18 years of age. Since then he has been a steel worker here.

Two years ago he noticed some numbness in the left arm. For the past eighteen months he has frequently burned this arm, sometimes severely. There has been no pain associated with these burns. Three months ago his attention was drawn to a white spot on the outer aspect of the left arm, and for the past two months he has noticed other similar lesions.

The patient presents an eruption made up of scattered macules of varying sizes up to 12 or 15 cm. in diameter. The largest lesions are found on the outer aspect of the left arm, the lower part of the lumbar area and the anterior aspects of the thighs. The individual lesions show depigmentation, and at the periphery of a few there is slight hyperpigmentation. There is no definite atrophy, nor is there a loss of any of the cutaneous appendages. In the areas involved there is a loss of perception of pain and temperature. There is an enlargement of the peripheral nerves—particularly of both ulnar nerves—and these are nodular.

The Wassermann reaction was negative. Sections from the skin and from the right ulnar nerve are presented. Staining for acid-fast bacilli showed many such organisms in the nerve.

DISCUSSION

DR. L. R. TAUSSIG: Dr. Novy brought the section from the skin to the clinic over a month ago. The sections did not show a structure suggestive of leprosy. As far as the histologic structure is concerned, the lesion appeared to be toxic. The stain for acid-fast bacilli failed to show any. Later he obtained a piece of nerve, and this, as is apparent, was laden with acid-fast bacilli. I then restudied the original section on which a stain for acid-fast organisms had been used and was able to find a few lepra bacilli.

Sycosis Vulgaris. Presented by THE DIVISION OF DERMATOLOGY OF THE UNIVERSITY OF CALIFORNIA MEDICAL SCHOOL.

Tertiary Syphilis: Destructive and Gummatous Involvement of the Naso-Palatine-Pharyngeal Structures. Presented by THE DIVISION OF DERMATOLOGY OF THE UNIVERSITY OF CALIFORNIA MEDICAL SCHOOL.

NEW YORK DERMATOLOGICAL SOCIETY

EUGENE F. TRAUB, M.D., *President*

Oct. 26, 1937

FRANK C. COMBES, M.D., *Secretary*

Acrodermatitis Chronica Atrophicans (Preatrophic Boggy Infiltrations). Presented by DR. FRED WISE.

Miss G. R., aged 45, a bacteriologist, first noticed red, elevated, soft swellings of the legs one and a half years ago. She states that they appeared after exposure to severe cold weather. There were no subjective symptoms.

Examination on July 15, 1937, showed a group of dusky red, infiltrated, slightly elevated, somewhat elastic lesions on the left leg and the right thigh. These swellings were from the size of a dime to that of a silver quarter; the edges were ill defined and merged with the normal skin. Similar lesions in much smaller numbers were present on the right thigh. The right leg exhibited no inflammatory lesions, but there was a suggestion of atrophic skin, with prominent superficial veins. There was no clinical evidence of atrophy in the infiltrated lesions, but the histologic report showed changes corresponding with those characteristic of the early nodular lesions of acrodermatitis chronica atrophicans.

DISCUSSION

DR. HOWARD FOX: I am not familiar with a nodular eruption that precedes the atrophic patches of acrodermatitis chronica atrophicans. The lack of symmetry shown in this case is unusual for acrodermatitis.

DR. GEORGE M. MACKEE: At present the condition does not look like what is always recognized as acrodermatitis chronica atrophicans. I never saw the disease begin with nodules, but as I can make no other diagnosis and Dr. Wise states that cases with such an onset are reported in the literature, I must accept the diagnosis, at least tentatively.

DR. EDWARD R. MALONEY: I agree with what Drs. Fox and MacKee have said. They have expressed my ideas of this case.

DR. R. H. RULISON: I agree with the previous speakers.

DR. A. BENSON CANNON: The lesions have the appearance of granuloma, the nodules resembling erythema nodosum of tuberculous origin. I suggest a thorough investigation of the case for tuberculosis, the study to include histologic sections, inoculation of guinea pigs with some of the tissue removed and a tuberculin test.

DR. FRED WISE: In a search of the literature I found references to thirteen articles describing the so-called preatrophic infiltrations of the legs. These have preceded the usual atrophic changes in a number of cases of acrodermatitis atrophicans. Sections from this patient were examined by three pathologists, one of whom rendered the diagnosis of an "early stage of acrodermatitis atrophicans," without being cognizant of the clinical diagnosis. The other two pathologists confirmed the clinical diagnosis. These infiltrative, more or less boggy lesions are not to be confused with the late periarticular fibrotic nodules described by Oppenheim and later by Ketron and me. There is no evidence of tuberculosis or another form of granuloma in the sections.

DR. EDWARD R. MALONEY: May I ask Dr. Wise how long this "pre" stage lasts?

DR. FRED WISE: Some of the preatrophic lesions persist for years before clinical evidence of atrophy becomes manifest.

American Leishmaniasis of Generalized Type. Presented by DR. HOWARD FOX.

R. M., a man aged 43, an employee of an oil company, has worked in the "bush" in Venezuela for the past ten years. Early in January 1937 he was bitten by innumerable sand flies; high fever developed; he suffered from malaise, and there were congestion of the conjunctivae, generalized pains and a blood count of 4,400 leukocytes, with a relative lymphocytosis. The fever lasted two days. Two weeks later an eruption appeared, which gradually became generalized. The blood count showed normal amounts of red cells and hemoglobin and mild leukopenia. The patient was hospitalized on January 25. He suffered from moderate fever, which subsided at the end of two weeks. Examinations of the blood for malaria and repeated Kahn tests gave negative results. While in the hospital he was treated with salicylates, neoarsphenamine, potassium iodide, calcium, vaccines and a derivative of sulfanilamide. He was given ultraviolet therapy, and numerous lotions and salves were applied.

The patient was first seen by me on May 4, 1937, at which time the eruption had been present for ten months. It was generalized, symmetrical and fairly profuse, a hundred and thirty lesions being present. It affected chiefly the face and the extensor aspects of the extremities and to a slight extent the mucous membranes of the nose, the mouth and the throat. The cutaneous lesions varied in size from that of a pea to that of a horse chestnut and were sharply demarcated and surrounded by an edematous areola. They were reddish, semisolid and as a rule devoid of pain and tenderness. The majority of the lesions were covered with adherent crusts, the central portions of many being ulcerated. After the crusts had fallen and the ulcers had healed, reddish depressed scars remained. There were a few superficial ulcerations on the nasal septum and the gums and one lesion on the hard palate; all of these were painful and tender. The general appearance of the eruption at the time of examination strongly suggested bromoderma or iododerma. There was no history, however, of ingestion of these drugs, and their appearance was not detected in the urine. Histologic examination of one of the lesions showed a granulomatous structure which did not suggest either syphilis or tuberculosis. Smears from the ulcers failed to show the presence of Leishmania. Cultures were not made, as suitable mediums were not available at the time. The patient was given twenty-two injections of antimony and potassium tartrate, and the entire eruption has now disappeared, the majority of the lesions having left depressed scars. The general health is now good.

DISCUSSION

DR. HOWARD FOX: I think any factitious element can be excluded, as the eruption was symmetrical on the arms and the legs and involved the mucosa of the nose and the throat. This picture is not the usual one for the American type of leishmaniasis, in which there are only three or four ulcers of various sizes. The condition is strikingly similar to that in a case I reported during a study of leishmaniasis in Brazil. Although Leishmania was not found in smears in this case, the diagnosis of leishmaniasis is reasonably certain from the history of numerous bites by phlebotomi in a region where leishmaniasis is endemic, from the invasion of the mucous membranes and from the favorable response to antimony and potassium tartrate. Syphilis, tuberculosis and an eruption due to bromides or iodides can apparently be excluded.

DR. J. GARDNER HOPKINS: How difficult is it to find the parasite?

DR. HOWARD FOX: I was told by my Brazilian colleagues that it was easier to demonstrate the organism by culture than by microscopic examination of smears.

A Case for Diagnosis (Severe Pitting, with Depigmentation and Hyperpigmentation). Presented by DR. FRED WISE.

Miss R. L., aged 18, a secretary, has an itching papular eruption which began on the upper part of the back three years ago. Groups of small papules, capped by adherent crusts, spread to the middle and the lower portion of the back and the arms. At the time of examination, on June 19, 1937, only a few scattered crust-covered papules were seen on the upper part of the back. There were no evidences of scratching. The entire upper and middle portions of the back and the upper part of the chest presented a widespread mottled hyperpigmentation, in the midst of which were innumerable, slightly depressed, lentil-sized scars, which appeared, by contrast, to be depigmented. The arms and the shoulders were similarly affected. The pigmentation appeared before arsenic had been administered. A drug eruption was ruled out. The papular element disappeared after a series of intravenous injections of sodium thiosulfate. The patient's general health has always been good.

DISCUSSION

DR. GEORGE M. MACKEE: The case might be one of dermatitis herpetiformis, the pigmentation being due to the disease and the arsenic or both and the scarring to the scratching and infections.

DR. PAUL E. BECHET: It would be hard to conceive of dermatitis herpetiformis as extensive as this eruption and located on the chest and the back only. There are many lesions. Some are almost confluent. As Dr. MacKee said, the diagnosis is a matter of conjecture. My suggestion would be that this condition is ordinary acne, which has been scratched repeatedly for years. In the pruritus accompanying pediculosis corporis a similar pigmentation due to scratching is often seen. My guess is that the patient has ordinary folliculitis or acne and either scratches herself or has some one do it, thereby causing this extensive scarring and pigmentation.

DR. R. H. RULISON: I cannot get rid of the idea that there is some factitious element here. I do not know how the lesions are produced, and I have no diagnosis to offer.

DR. FRANK C. COMBES: I cannot agree with either of the diagnoses that have been suggested, namely, acne and dermatitis herpetiformis. In the lumbar region the patient has perfectly clear skin. The lesions on the upper part of her back do show hyperpigmentation, but there seems to be some depigmentation. The depigmented areas have their convex borders toward the hyperpigmented areas. The scarring is in the apparently depigmented areas. However, I cannot offer any diagnosis except dyschromia.

DR. A. BENSON CANNON: If the presenter had not ruled out the possibility of self-inflicted wounds, I should suggest it as a probable cause of the trouble.

The location, the distribution and the character of the blood-crusted excoriated lesions, with a mingling of scarring, are most suggestive of neurotic excoriations.

DR. FRED WISE: The pigmentation was present long before treatment with arsenic was commenced.

A Case for Diagnosis (Rosacea-like Tuberculid of Lewandowsky? Acne Varioliformis?). Presented by DR. EUGENE F. TRAUB.

H. L., a man aged 56, was first seen on Aug. 24, 1937, at which time he had an eruption on his face which had begun about six or seven years previously. The lesions had appeared occasionally on the scalp and rarely on the chest. He has been under more or less constant medical attention since the onset of the condition, which appeared as a small papulopustular eruption terminating in central necrosis and crusting and healed, leaving tiny, pitted scars. At first he was given numerous treatments with roentgen rays and a large course of ultraviolet treatments, and he used many types of ointments and lotions. He has received a large number of injections, the nature of which he does not know. His tonsils were removed, and his teeth have been carefully checked, as have all other possible foci of infection. Everything at the present time is reported as normal. While the scarring is not immediately evident when the patient's face is examined, this is probably due to the facts that it is so profuse and that each lesion leaves only a shallow fresh scar. Therefore, unless the light strikes the face in such a way as to cast a shadow, it is difficult to see the pitting. While the patient has been under my observation, no lesions have been observed on the chest, but there have been a number of similar lesions on the scalp.

The Wassermann test and urinalysis showed no abnormality. One pathologist made a diagnosis of rosacea-like tuberculid after examination of a small piece of tissue removed from the scalp, while another reported that the condition was acne varioliformis. A third pathologist suggested that the section showed features of a tuberculid reaction with necrosis of the epidermis. He stated that this was uncommon in rosacea-like tuberculid. The description of the histologic section was as follows: There was marked destruction and vesiculation about the hair follicles. The vesicle was filled with serum. There was no evidence of pustulation. There was an inflammatory exudate in the upper part of the cutis, largely of the round cell type. There were some giant cells of the Langhans type.

DISCUSSION

DR. PAUL E. BECHET: I did not see any rosacea-like lesions. There seemed to be some small papules on the forehead, at the hair line and on the temples and some extremely superficial varioliform scarring. I should be much more inclined to consider a mild type of acne varioliformis as the correct diagnosis.

DR. GEORGE M. MACKEE: I do not think there is enough of an eruption present to allow one to make a diagnosis.

DR. EDWARD R. MALONEY: I think the histologic picture does not fit in with the diagnosis of rosacea-like tuberculid. There are a few giant cells of the Langhans type, no epithelioid cells and just a small round cell infiltration. I do not think that is enough evidence to justify a diagnosis of rosacea-like tuberculid.

DR. J. FRANK FRASER: One cannot make a diagnosis of rosacea-like tuberculid from this histologic report. Giant cells frequently occur in cases of indurated acne and rosacea. The report as read did not in my opinion harmonize with the diagnosis of rosacea-like tuberculid.

DR. EUGENE F. TRAUB: Tuberculin tests have not been done. There was a difference of opinion among several pathologists who examined the section as to whether the process was acne varioliformis or rosacea-like tuberculid. It is possible, because a tiny punch was used, that the specimen may not have shown the characteristic features needed for a conclusive diagnosis. My first impression was that this case was one of acne varioliformis, and it is perfectly possible that

this impression is the correct one. On the other hand, the close clinical resemblance of the lesions on the face to rosacea makes it perfectly possible that they might be rosacea-like tuberculid. The condition is one which definitely terminates in scarring, so that the ordinary conditions like rosacea or folliculitis, which was the diagnosis under which he was treated before, were obviously not correct. An antiseptic ointment which he has used has given him about as much relief as any form of treatment tried to date.

Dermatitis Herpetiformis. Presented by DR. EUGENE F. TRAUB.

K. S., a woman aged 69, a private patient, was first seen in June 1935, at which time she had several erythematovesicular patches scattered over the left leg. She stated that she had had some type of eczematous eruption for twelve years. A diagnosis of eczema was entertained at that time, and the eruption disappeared promptly after a few exposures to roentgen rays. During the next two years she was seen during a number of recurrences, all of which suggested dermatitis of external origin or a patchy, weeping, orbicular eczema. It was not until the fall of 1936 that the eruption took on a different character and suggested bullous toxic erythema, some of the lesions actually being urticarial. The diagnosis of dermatitis herpetiformis suggested itself, and the patient has been observed from this standpoint since that time. She has presented a grouped multiform eruption consisting of erythema, wheals, vesicles and blebs, all of which were intensely pruritic. The eruption healed, with slight pigmentation but no scarring. Usually, after treatment for about two months a remission has taken place, only to be followed in a short time by a relapse. The present attack is the worst that the patient has suffered, and for the first time large bullae have appeared, some of them on the legs measuring from 1 to 1½ inches (2.5 to 3.8 cm.) in diameter. She was given solution of potassium arsenite by mouth and iron cacodylate intravenously. She tolerated arsenic badly, however, and the picture is partly masked today by an arsenical dermatitis and edema of the face and the extremities. Repeated examination of the urine has shown no abnormality. The patient is slightly anemic, but otherwise the condition of the blood is normal.

DISCUSSION

DR. FRED WISE: I have believed that I observed improvement from repeated injections of sodium thiosulfate in cases of Duhring's disease.

DR. A. BENSON CANNON: The dermatitis is so universal that it obscures any appearance of dermatitis herpetiformis. The only other lesions are a few urticarial papules on the back and the sides. The patient's known intolerance to arsenic in various forms and the aggravation of the dermatitis after injections of arsenic would make me think of arsenical dermatitis. The patient's blood, urine and skin should be examined for arsenic before treatment for dermatitis herpetiformis is instituted. Because of the duration and the intense itching of the cutaneous eruption and the few urticarial lesions, one might want to rule out the possibility of mycosis fungoides, although I think that diagnosis unlikely.

DR. HOWARD FOX: I suggest that the patient be hospitalized and given fever therapy, together with soothing antipruritic applications.

DR. PAUL E. BECHET: I suggest trying nonspecific protein therapy.

DR. GEORGE M. MACKEE: I accept the diagnosis of dermatitis herpetiformis, because the presenter has observed a number of exacerbations, some of which were, he states, typical of that disease. But I should not be willing to make a diagnosis of that disease on the strength of the present eruption. One must think of erythema multiforme, drug eruption and mycosis fungoides. If it is assumed that the condition is dermatitis herpetiformis, colloidal manganese might be tried.

DR. EUGENE F. TRAUB: The diagnosis seems beyond doubt in this case at the present time; although the disease did not manifest itself in any characteristic way until about two years ago, since that time all the features necessary to this diagnosis have been present. There have been decided grouping and multiformity,

consisting of erythema, wheals, vesicles and large blebs, with intense itching which cannot be controlled satisfactorily with either local or internal medication. There are remissions and relapses, the old lesions leaving slight pigmentation. Only mycosis fungoides might be considered on the basis of the intense itching, but I have never seen a prefungoid eruption with blebs on an absolutely normal skin, such as this patient frequently manifests. As I stated in the history, the picture tonight is somewhat masked, owing to the arsenical dermatitis from which she is suffering. For the past two or three weeks she has been receiving injections of sodium thiosulfate, but there has been no noticeable improvement.

Poikiloderma (Civatte). Presented by DR. FRANK C. COMBES.

M. V., a woman aged 27, presents an eruption limited to her face, the sides of her neck and, recently, the backs of her hands and the forearms. It extends to the upper part of her chest, forming a line corresponding to the upper limit of her dress. It consists essentially of a network of telangiectases and a faint dusky brown pigmentation. There is no apparent atrophy. She has not been excessively exposed to the sun, since her skin burns readily and does not tan.

DISCUSSION

DR. EUGENE F. TRAUB: This condition does not impress me as poikiloderma of Civatte but seems rather to be hypersensitivity to sunlight. I saw no true atrophy or marked pigmentation but only telangiectatic spots. Such vascular changes are common on the V neck front of a woman's chest, the sides of the neck and the back, where the dress is cut out, exposing the skin to sunlight.

DR. PAUL E. BECHET: The patient told me that she was extremely sensitive to sunlight. Moderate exposure produces a severe reaction and even blistering.

DR. FRANK C. COMBES: This eruption is of seven years' duration. Its onset was rather gradual. It is true that the patient does not tan, but she does not expose herself unduly to the sun for that reason. There are many people who do not tan but in whom this type of lesion and telangiectasia do not tend to develop. I shall admit that there is no apparent atrophy, but there is some slight pigmentation. As regards the time element, I agree that poikiloderma of Civatte usually develops rapidly, and in this case it has been rather long in development. However, the cases which have been accepted as of the same type as Civatte's original cases have varied considerably, and I think the condition is not a well defined entity.

Scleroderma and Hypertrichosis in a Child. Presented by DR. EDWARD R. MALONEY.

W. J., a girl aged 5 years, born in the United States, presents a linear patch of scleroderma behind and below the left ear and wider at the lower end. The ear itself is involved. This eruption began two years ago, after an attack of measles.

The extensor surfaces of the upper extremities and, to a lesser degree, the extensor surfaces of the lower extremities, the upper part of the back, the region over the spine and that over the sacrum are covered with long dark, fine hairs. This hypertrichosis has been present since birth.

DISCUSSION

(The members agreed unanimously with the diagnosis.)

A Case for Diagnosis (Larva Migrans? Erythema Circinatum?). Presented by DR. J. FRANK FRASER.

A. S., a boy aged 2 years, was first seen at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Oct. 26, 1937, with an eruption on the buttocks, the abdomen and the back of two weeks' duration.

On the affected areas there is a slightly pruritic erythematous eruption in pencil streak formation. It began on the buttocks, spread to the abdomen and then to the back and is now beginning to fade from these areas in the same order.

DISCUSSION

DR. J. FRANK FRASER: The patient was first seen this morning. Dr. Tenney suggested the diagnosis of larva migrans. When questioned, the mother said the child had never been away from the city or on the beach. She changed the story tonight and stated that the child was on the beach at Coney Island in July but that the eruption did not appear until three weeks ago. The case is presented for diagnosis.

DR. H. H. WHITEHOUSE: I should think the condition is circinate erythema multiforme. I should hardly think it is larva migrans, since it appeared so long after the patient was on the beach. It does not itch.

DR. PAUL E. BECHET: It certainly does not resemble circinate erythema multiforme. All the classic symptoms of creeping eruption are present—the narrow threadlike red line, curved and looped, and even the history of lying on wet sand a few weeks prior to the appearance of the eruption coincides with Kirby-Smith's observation that the parasite is found in soft damp sand.

DR. HOWARD FOX: In my opinion, this is a classic example of creeping eruption. The patient presents a delicate pinkish threadlike elevation which advances day by day for a fraction of an inch. It has produced a curious pattern that is not simulated by any other disease. The unusual feature is that the patient does not complain of itching and that no scratch marks are visible. Most of the infestations seen in Florida are contracted at the seashore or in the interior of the state during rainy weather. Whether the larva is that of a fly or a nematode worm, I think it would be impossible to say by the appearance of the lesions. Larvae of nematode worms were found in 5 of Kirby-Smith's cases.

DR. R. H. RULISON: I agree that the condition is a creeping eruption.

DR. FRANK C. COMBES: I agree with Dr. Fox.

DR. FRED WISE: I agree with Dr. Fox.

DR. EDWARD R. MALONEY: I do not see how any diagnosis but creeping eruption can be made in this case. It is not at all necessary for the subject to go to a beach to get it. I have observed many cases in which the patient has not been near a beach for many months. The larva of the horse fly, particularly, can be responsible for this eruption. I did not see clinically that there is any other diagnosis to entertain but creeping eruption.

DR. A. BENSON CANNON: I agree with Dr. Fox.

Lupus Miliaris Disseminatus Faciei. Presented by DR. FRANK C. COMBES.

R. H., a man aged 28, in good health, presents on his lower eyelids and the upper parts of his cheeks a group of approximately a dozen shiny papules, ranging in diameter up to 5 mm. They are dusky red, and a few of them are tinged with yellow, with apical crusting. A few punctate punched-out scars mark the sites of previous lesions. One of these is located on the upper lip. The condition has been present for seven months. The reaction to the tuberculin (Mantoux) test was negative with dilutions of 1:100,000 and 1:10,000. The Wassermann reaction was negative.

DISCUSSION

DR. EDWARD R. MALONEY: I question the diagnosis. To me the lesions do not have the clinical appearance of lupus miliaris. Possibly that may be due to the light under which they are seen tonight. They lack the yellow color that they usually have. Another point is that the tuberculin test gave negative results with several dilutions. I think that is against the diagnosis of lupus miliaris

disseminatus faciei. I should think of the possibility of superficial cysts of some sort, but I do not think the case is one of lupus miliaris.

DR. ALBERT S. TENNEY, East Orange, N. J. (by invitation): I suggest the diagnosis of multiple benign cystic epithelioma. The lesions are pale and cystic.

DR. A. BENSON CANNON: I think the lesions are as yellow as gold. The location, the firmness and the spontaneous disappearing with scarring of some of the lesions are characteristic of the diagnosis as presented.

DR. J. FRANK FRASER: I agree with the presenter's diagnosis. The color, to my mind, is right for that condition. I should not want to make a positive diagnosis without a microscopic examination, however.

DR. HOWARD FOX: From the location and the appearance of the lesions and the age of the patient I think multiple benign cystic epithelioma is the most likely diagnosis. The lesions appear to me to be flesh colored rather than golden yellow.

DR. PAUL E. BECHET: I agree with Dr. Fox. I think the lesions belong to that group designated by many names, one of which is multiple benign cystic epithelioma.

DR. JOSEPH J. ELLER: I agree with Dr. Maloney's interpretation.

DR. GEORGE M. MACKEE: I agree with the diagnosis as presented. The condition does not look to me like benign cystic epithelioma. A number of lesions have disappeared spontaneously, leaving scars.

DR. FRED WISE: I agree with the diagnosis as presented.

DR. EUGENE F. TRAUB: My diagnosis in this case would be lupus miliaris disseminatus faciei.

DR. FRANK C. COMBES: No microscopic examination has been performed, because of the danger of ectropion. The negative reaction to tuberculin is a minor point in favor of the diagnosis of lupus miliaris disseminatus. As regards the color, the lesions are dusky red, not skin colored by any means, and there are a few crusts on some of the lesions which would not be expected in benign cystic epithelioma. There is a yellowish tinge to some of the lesions, particularly on diascopic pressure.

Histiocytoma Cutis. Presented by DR. EUGENE F. TRAUB.

G. W., a woman aged 34, was first seen at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Oct. 22, 1937. She presents an eruption consisting of nodules and tumors on the arms, the legs and the back. On the arms there are several discrete nodules measuring about 1.5 cm. in diameter which are only slightly elevated above the surface of the skin but have considerable depth and slight central umbilication. On the back is a somewhat similar nodule, lacking, however, the button-like appearance of the lesions on the arm and presenting rather a rounded, dome-shaped elevation of dusky reddish brown. The lesions on the legs are of the size of tumors, and apparently several have become confluent to form a rather large irregular mass. The color varies from reddish to purplish brown, and the consistency of the lesion is firm or hard. The patient complains of slight pain in some of the lesions.

Because a number of well trained dermatologists looked on this case as one of sarcoid of Boeck—a mistake, incidentally, commonly made when the patient presents only a few lesions of this type—I wish to draw this condition again to the attention of the members.

Several of the lesions were removed for microscopic study, and a microscopic diagnosis of fibroma and histiocytoma with hemorrhage was made. A section from the fibroma showed a growth of fibroblasts in strands and whorls. A section from the histiocytoma showed a growth of fibroblasts in strands and whorls. The blood vessels on the upper surface of the lesion were increased in size and quantity, and throughout the growth there were numerous multinucleated

cells, usually of the foreign body type. In the upper portion of the growth there was a hemorrhage into the tissue, and many of the cells carried dark brown pigment. Perles' test gave positive results. On the basis of one section a diagnosis of fibroma with multinucleated lipoidal histiocytes was made, and another section showed a process of the type of noduli cutanei.

DISCUSSION

DR. J. FRANK FRASER: I feel certain that these nodules will show the histologic structure of neurofibroma.

DR. R. H. RULISON: I think the condition is typical of neurofibroma.

DR. EDWARD R. MALONEY: I agree with Dr. Fraser.

DR. EUGENE F. TRAUB: By neurofibroma, Dr. Fraser, you probably refer to the condition sometimes described as dermatofibroma or noduli cutanei, do you not? Recently, the cases previously classified under the headings dermatofibroma, noduli cutanei and a number of similar ones have been more correctly classified under the title histiocytoma cutis.

Radiodermatitis Superimposed on Pustular Psoriasis(?) or Dermatophytosis(?). Presented by DR. EUGENE F. TRAUB.

S. K., a woman aged 37, a housewife, has been under observation since September 1937 because of an eruption on the hands and the feet of five years' duration. During this period there have been no remissions, and the eruption, which is on a slightly erythematous base, consists of small pustules. Even in the early stages the lesions seem pustular rather than vesicular, but it is possible that some of them actually were vesicular at the onset. The patches have been exceedingly persistent and rebellious to all forms of treatment. The patient has been given a large number of treatments with roentgen rays (19, with short intervals between treatments), so that on the left hand, especially about the thumb, there are some atrophy and telangiectasia. Mycologic examinations have repeatedly given negative results, and the reactions to trichophytin and to oidiomycin tests were negative. A section was removed for microscopic study, and a microscopic diagnosis of dermatophytosis was made. The section showed a large tense vesicle filled with inflammatory exudate within the epidermis. There was a thick crust, the rest of the epidermis being normal. There was some dilatation of the blood vessels of the papillary body and a marked inflammatory exudate in the corium under the vesicle. The methylene blue stain showed no fungi.

DISCUSSION

DR. GEORGE M. MACKEE: My tentative diagnosis in this case is pustular psoriasis.

DR. EDWARD R. MALONEY: I agree with the diagnosis of pustular psoriasis.

DR. EUGENE F. TRAUB: It was my impression that this case was one of pustular psoriasis, and everything fitted into this picture with the exception of the histologic observations.

Sarcoid, Sclerodermatiform Tuberculous Type (Gougerot). Presented by DR. R. H. RULISON.

E. K., a white woman aged 44, a widow born in Ireland, was first seen in the department of cutaneous diseases of the Lincoln Hospital in February 1937, because of dermatophytosis of the feet and the fingers. At subsequent visits she complained that for the past five years she had had yellowish lumps on the lower parts of the legs, without subjective symptoms. She stated that she had sustained moderate trauma to one shin, without any break in the skin. She considered herself in good health, aside from occasional asthmatic attacks following colds. Her husband died in 1931 of pulmonary tuberculosis.

On the anterior aspect of the lower part of the right leg is a palm-sized, irregularly outlined, yellowish and reddish, mottled, smooth, slightly scaly, infiltrated plaque. The periphery has a narrow violaceous band. Numerous minute telangiectases are visible throughout the lesion. The entire plaque is hard but not so hard as scleroderma. Below the right knee is a more recent, reddish and violaceous markedly infiltrated deep-seated nodular lesion the size of a half-dollar. On the lower part of the left leg there is a lesion similar to but smaller than the one on the lower part of the right leg. Yellowish and brownish pigmented lesions are present on the anterior aspect of the left leg. Marked deep and superficial varicosities, together with slight edema of the ankles, are found on both legs. On the dorsa of both feet there are reddened, scaly, crusted eczematous changes. Scaling and maceration between the toes and thickening and yellowish discoloration of the toe nails are noted.

Roentgenograms of the legs showed no abnormalities of the lower two thirds of the tibia and the fibula. Urinalysis showed no abnormalities. Histologic examination by Dr. Benzion Liber of the lesion on the upper portion of the right leg showed densely fibrotic tissue in which were numerous areas of infiltration of masses of lymphocytes, in the center of which were round areas of incipient necrosis, with epithelioid cells and, occasionally, giant cells of the Langhans type. Staining with iodine showed no amyloid reaction anywhere in the sections. A stain for fat revealed a small amount of subcutaneous fat persisting between fibrous areas. A polarizer showed that there was no doubly refractile lipoid. A microscopic diagnosis of granuloma of the hypoderm, probably tuberculous, was made. This corresponded with nodular sarcoid or erythema induratum.

The case is presented as one of sclerodermatiform tuberculous sarcoid (Gougerot).

DISCUSSION

DR. FRED WISE: I agree with the diagnosis presented by Dr. Rulison.

DR. GEORGE M. MACKEE: I agree absolutely with the diagnosis as presented.

DR. PAUL E. BECHET: I should like to know how Dr. Rulison differentiates this condition from ordinary scleroderma. Clinically, the patch so strongly resembles localized scleroderma that I could make no other diagnosis.

DR. HOWARD FOX: I agree with the diagnosis and would say that this case furnishes another example of how varied the types of sarcoid may be, ranging from a few small macules to tumors of various size.

DR. EDWARD R. MALONEY: The histologic examination shows the upper lesion to be sarcoid. The lower lesion, which is now sclerodermatous, started, according to the patient's history, in the same way as the upper one. Therefore, I agree with the diagnosis as presented.

DR. EUGENE F. TRAUB: I have had 2 cases in which the picture was exactly similar to and another in which it closely resembled that in this one. In all there was the same histologic appearance, a tuberculoid structure with some of the features of morphea. Examinations of the blood and the urine for sugar and dextrose tolerance tests were done in these cases, but no evidence of diabetes was found. The only conclusion that could be reached was that the condition was some type of sarcoid, perhaps associated with morphea, as Dr. Rulison has suggested.

A Case for Diagnosis (Papulonecrotic Tuberculid?) (Recurrent Purpura of the Mucosa and the Skin). Presented by DR. FRED WISE.

Miss B. F., aged 32, born in the United States, an office clerk, is presented for the diagnosis of a disease of twenty-five years' duration. The disease began with the appearance of circumscribed hemorrhages, varying in size from that of a pea to that of a bean, in the mouth, involving the gums, the buccal mucosa and the lips at different times. These eruptions were preceded by attacks of chills and elevations in temperature up to 101 F. The lesions were so painful that only

soft foods could be eaten. After an interval of two or three weeks the lesions subsided without treatment. In the past twenty-two years similar hemorrhagic spots made their appearance at irregular intervals, chiefly in cold weather, on the extremities. Histologic examination of a pea-sized hemorrhagic spot on the leg showed a structure resembling papulonecrotic tuberculid.

During the past six months the patient has had eruptions of isolated purpuric crops on the soles, the arms and the legs. These disappeared spontaneously, leaving small depressed scars on the legs. In the past month hemorrhagic lesions have appeared on the lips, the buccal mucosa and the left thigh. These were accompanied with chills, fever and dizziness. The lesions on the lips have left superficial scars.

Examination shows on the right side of the lower lip a dark reddish purple hemorrhagic lesion, about the size of a dime, which is painful and tender. The duration of this isolated lesion has been four days.

Laboratory investigations included tuberculin tests, blood counts, chemical examination of the blood, roentgenograms of the chest, Wassermann tests, bacteriologic examinations of the buccal and the labial lesions and determinations of the sedimentation rate of the blood. None of these showed any abnormality. Physical examination showed chronic nasopharyngeal catarrh, but the findings were otherwise irrelevant.

DISCUSSION

DR. GEORGE M. MACKEE: I suggest the diagnosis of papulonecrotic tuberculid and Sutton's periadenitis mucosa recurrens.

DR. R. H. RULISON: I think the condition is some sort of hematogenous infection with sudden flare-ups.

DR. FRED WISE: All the lesions were followed by scars and preceded primarily by hemorrhages. I cannot accept the diagnosis of papulonecrotic tuberculid associated with purpura because I saw the purpuric lesions on the day they appeared and they were true hemorrhages. That is not the way papulonecrotic tuberculid begins. This condition may be some obscure type of tuberculosis.

A Case for Diagnosis (Rosacea? Papulonecrotic Tuberculid?). Presented by DR. PAUL E. BECHET.

M. S., a woman aged 38, was first seen at the clinic today. She states that her eruption is of four years' duration and first appeared on the left cheek, remaining confined to that area for three and one-half years. The right cheek and the nose did not become involved until six months ago. There is no history of ingestion of drugs. The patient's nose and the adjacent areas of the cheeks are covered by a sharply outlined rather symmetrical deep red patch. Throughout the patch are papules, some of which are nodular and others crusted. There are many pitted scars throughout the lesion. The pits extend to the edges of the lesion only.

DISCUSSION

(DRS. HOWARD FOX, GEORGE M. MACKEE and EUGENE F. TRAUB considered the eruption to be ordinary rosacea.)

DR. PAUL E. BECHET: I cannot conceive of rosacea so sharply marginated, with punctate atrophic scarring limited to the areas of the disease. The disease extends over the zygoma almost to the temple, which is most unusual for rosacea. There is no telangiectasia—only superficial papules with a tremendous amount of erythema—and there are no pustules. I still greatly favor the diagnosis of papulonecrotic tuberculid.

Molluscum Contagiosum Simulating Verruca Plana. Presented by DR. PAUL E. BECHET.

M. C., a woman aged 24, has had an eruption limited to the backs of her hands for six months. New lesions have appeared from time to time during

this interval. On the dorsum of each hand there are numerous pinhead-sized papular lesions. Some of them are pinkish red. Viewed superficially, some of them are flat, strongly resembling flat warts, but when carefully inspected with a lens, a considerable number of them are characteristically elevated, waxy, rounded and button-like, with a central opening, but all of them are unusually small.

Lupus Erythematosus Bullosus of the Scalp. Presented by DR. J. FRANK FRASER.

H. E., a man aged 43, was first seen at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Sept. 9, 1937, with an eruption on the scalp of ten months' duration. The patient had a small sore above the forehead, which was diagnosed as ringworm and treated with roentgen rays. He has been treated with ultraviolet rays. After the roentgen treatments the lesions spread. The lesions have been treated with trinitrophenol and Aloe vera ointment, and many salves and lotions have been used.

At the present time the patient presents 1 large and 1 small red crusted patch on the top of the scalp. At one time definite Nikolsky signs were elicited in two areas on the scalp. There are no lesions elsewhere.

The Wassermann and the Kahn test were negative. Urinalysis showed no abnormality. Histologic examination showed some of the characteristic features of lupus erythematosus. There was no evidence of pemphigus.

DISCUSSION

DR. FRED WISE: I agree with the diagnosis. I observed the case previously, when the clinical diagnosis was more evident than it is now.

DR. GEORGE M. MACKEE: I agree with the diagnosis.

DR. HOWARD FOX: This diagnosis is correct in my opinion, because in the few cases I have observed there has been the same characteristic bullous eruption, healing with superficial atrophy.

DR. J. FRANK FRASER: The basic features of lupus erythematosus were present in the histologic picture, notably the loss of elastic tissue.

A Case for Diagnosis (Tuberculosis Cutis? Hydradenitis Suppurativa Destruens?). Presented by DR. EUGENE F. TRAUB.

F. J., a Negro aged 48, was first seen in October 1937, with an eruption in the axillae and the groins which he said was of twenty years' duration. Both axillae presented masses of gnarled and cordlike scar tissue, together with boggy swellings, from some of which a seropurulent material was being discharged. Small fistulous tracts were seen. The patient could raise his arms to his shoulders, elevating them only with the greatest of difficulty; at times, when the process became acute, it was impossible to raise the arms at all. The process in the groins was similar and consisted of abscesses exuding pus, swollen lymph nodes, old healed areas of fibrosis and scarring. The process was foul smelling and actually crippling, because the patient could walk only with difficulty.

DISCUSSION

DR. HOWARD FOX: A few months ago I saw 2 other patients at the Veterans Administration Facility because of lesions in the axillae and the groins similar to those presented by this patient. The appearance was that of scrofuloderma, which is usually seen in the neck in younger patients. The lesions of 1 of these men were apparently proved to be tuberculous.

DR. A. BENSON CANNON: I think this case is one of purulent infection. One might consider the condition's being due to an anaerobic streptococcic infection, as in the cases described by F. L. Meleney (*Ann. Surg.* **101**:997 [April]

1935). Two patients exhibited before this society with a diagnosis of scrofuloderma were later seen by Dr. Meleney, who diagnosed the condition as streptococcic infection and cured it by appropriate surgical asepsis. Certainly conditions of this type are not unusual in hospital practice, and they almost invariably prove to be purulent infections rather than tuberculosis. I should advocate surgical asepsis.

DR. ALBERT S. TENNEY, East Orange, N. J. (by invitation): I agree with Dr. Cannon. It seems to me that the primary lesion is suppurative folliculitis which has spread.

DR. FRANK C. COMBES: I agree with the remarks of Dr. Cannon. Incidentally, if this condition appeared on the scalp it would be called perifolliculitis capitis abscedens et suffodiens. I do not see why similar lesions cannot occur in other regions of the body in which hair and glands are similarly well developed.

DR. FRED WISE: Can the end-results of granuloma inguinale be excluded in a case of this kind?

DR. GEORGE M. MACKEE: My impression is that the condition is caused by pyogenic organisms, and I agree that the treatment is essentially surgical. The man has many sinuses which ought to be freely opened and drained, after which wet dressings should be applied.

DR. H. H. WHITEHOUSE: I agree with Dr. Cannon's interpretation. The condition needs surgical treatment.

DR. EUGENE F. TRAUB: I should have thought that this case was one of simple pyogenic infection had it not been for the fact that the patient had been studied thoroughly at the Veterans Administration Facility, where 1 or 2 other patients were similarly affected. It was the patient's understanding that because of tests performed there the process had been looked on as tuberculous. He thought that inoculations of animals had been done, and although he was not certain, he believed their results had been positive. It was my impression that if these areas were thoroughly cleaned out surgically and wet dressings of zinc peroxide applied, this patient might be cured of his condition.

DR. HOWARD FOX: In answer to Dr. Wise's question, I would say that at no stage does granuloma inguinale resemble scrofuloderma. The ulcers of granuloma inguinale are usually beefy red, usually have no crusts and have a well demarcated, slightly elevated and rolled border. The disease never invades the lymphatic glands and is largely confined to Negroes. It would be most unusual to see this disease in the axillae.

Ulcerating Nodular Syphilid. Syphilis of the Pylorus? Purpura. Presented by DR. HOWARD FOX.

E. J. R., a man aged 39, was wounded on the right side of the forehead by shrapnel during the World War. A year later three ulcers appeared in the neighborhood of the original lesion. The eruption gradually spread downward over the middle two thirds of the face and has consisted of nodules, which have broken down and ulcerated, many of them healing and leaving soft, depressed and pliable scars. At present there is an irregular, depressed scar at the right side of the forehead and a fairly symmetrical eruption of the nose, the cheeks and the chin, consisting of whitish, soft, depressed, sharply defined scars with a tendency to become confluent. The distal half of the nose has been destroyed and still shows redness and crusting. On the extensor aspect of the right forearm there is a group of sharply defined, confluent, whitish scars. On the lower extremities there is a symmetrical eruption of reddish macules varying in size from that of a pinhead to that of a small pea; these do not disappear when pressure is applied. The eruption has been present for about three weeks. Three months ago a similar eruption appeared on the legs and lasted several weeks. Three years ago the patient had vague gastrointestinal symptoms, which consisted of "gagging," vomiting and a sense of fulness in the epigastrium a half hour after meals.

The Wassermann reaction was strongly positive. A blood count showed 2,800,000 red blood cells, 70 per cent hemoglobin and 5,350 white blood cells. A roentgenogram of the stomach showed considerable narrowing and irregularity of the pyloric antrum, the appearance being definitely that seen in association with organic disease. The roentgenologist thought that syphilis was a possible cause of these changes. For the past ten years the patient has been treated by a number of general practitioners, with various ointments and ultraviolet rays. No one apparently suspected the syphilitic nature of the eruption. The patient was told by several doctors that he had lupus vulgaris. Since he was admitted to the Bellevue Hospital two weeks ago, the active lesions on the nose have improved under antisyphilitic treatment.

DISCUSSION

(The members agreed unanimously with the diagnosis.)

Erythema Toxicum. Presented by DR. PAUL E. BECHET.

LOS ANGELES DERMATOLOGICAL SOCIETY

THOMAS W. NISBET, M.D., *Chairman*

Oct. 12, 1937

CHARLES R. CASKEY, M.D., *Secretary*

Arsenic-Resistant Syphilis. Presented by DR. NELSON PAUL ANDERSON and DR. RICHARD EVANS, Santa Barbara, Calif. (by invitation).

E. A., a white woman aged 33, was referred because of an eruption on her face. The lesions are dull purplish, with a slight tendency to scaling. In July 1936 she was treated with ultraviolet radiation for a lesion below the left eye. After this lesions developed generally over the face. The Wassermann reaction was found to be positive, and she was given three injections of neoarsphenamine at weekly intervals. The injections were discontinued, as no improvement was observed. No antisyphilitic treatment was given for nine months. The eruption has resisted fairly large and frequent doses of neoarsphenamine and of bismuth preparations. It was noted that after each injection of an arsenical a distinct local Herxheimer effect would occur in all the lesions. The patient, because of the early discontinuance of therapy, was originally harmed rather than helped by the few treatments she received. The events in this case explain an important factor in cases of arsenic-resistant syphilis.

DISCUSSION

DR. STANLEY ANDERSON: A patient under my care had primary and secondary lesions of syphilis in the latter part of 1936. The treatment at first was irregular, which probably contributed to the development of arsenic-resistant secondary lesions. I attempted to increase general resistance with a diet high in calories and vitamins, together with ultraviolet irradiation and the intravenous injection of typhoid vaccine. Arsphenamine was discontinued for eight weeks, and mercury and a bismuth preparation were given intramuscularly. During this procedure the lesions began to show slight improvement. Neoarsphenamine was then given, the intervals being shortened and the dosage increased, and satisfactory results were obtained. About six months was required for complete healing of the lesions.

DR. L. F. X. WILHELM: I remember an interesting case in New York in which the patient was careless in her treatment at the beginning. As a result, a resistant ulcer developed in the throat. This ulcer resisted arsphenamine, neo-

arsphenamine, a bismuth preparation and the iodides. The condition finally responded to fever therapy, and I understand that the lesions have completely healed.

DR. NELSON PAUL ANDERSON: Dr. Stanley Anderson tells me that he feels that the change to mercury may have been the deciding factor in bringing about improvement in his case. It is interesting that the serologic reaction of this woman's spinal fluid is definitely positive, although there are no other changes besides the positive Wassermann reaction.

A Case for Diagnosis (Lichen Planus? Lupus Erythematosus?). Presented by DR. KENDAL FROST.

E. V. Q., a white woman aged 41, states that she has had an eruption for about eighteen months. She had had various forms of treatment when first seen, including a series of injections of colloidal manganese. The eruption had improved somewhat but still involved the arms, the legs and the buttocks. The patient is moderately emaciated. On the forearms, the lower part of the back, the buttocks and the legs are grouped erythematous flat, angular papules, which have a more or less annular arrangement. In these areas are many atrophic spots of the same configuration, which represent healed lesions. In some places the apparent atrophy is being replaced by an almost normal-appearing skin, although some brownish discoloration remains in nearly all the previously involved areas. Her treatment has consisted of iodobismitol with saligenin semiweekly from April 30 to Aug. 10, 1937, and of 1/16 grain (0.004 Gm.) of mercury bichloride semiweekly from that time to the present. I think there has been about 50 per cent improvement in the active lesions. The patient was presented at the meeting in May 1937.

DISCUSSION

DR. H. C. L. LINDSAY: The condition certainly looks like lupus erythematosus; yet some parts resemble lichen planus. I wonder what the microscopic section showed.

DR. WILLIAM H. GOECKERMAN: I feel as I did before, that the diagnosis is not settled. There is definite improvement in the general condition of the patient. There has been improvement during treatment with the bismuth preparation, but that does not contribute anything to the diagnosis. I still should not put my vote down for either lichen planus or lupus erythematosus. The condition is one of those transitional forms for which a differential diagnosis is difficult.

DR. SAMUEL AYRES JR.: I feel as I did before, that it is rather difficult to be dogmatic. I favor the diagnosis of lupus erythematosus rather than lichen planus. There is something about the reticulated lesions of the legs that does not look like lichen planus, and according to the patient the lesions have not been especially itchy. I should be interested in knowing the histologic features of these reticulated lesions. They look like dull red streaks, like the sort of thing that appears when persons sit before a fire and bake their legs. I think there is a toxic element. I cannot see lichen planus.

DR. NELSON PAUL ANDERSON: I still believe the condition to be lupus erythematosus. I have never seen a patient with extensive lichen planus who was as sick as this patient. Patients suffering from lichen planus may have a marked and widespread eruption and still be in good physical condition. The fact that the condition has improved under metallic therapy is not significant. Such therapy might have helped either lichen planus or lupus erythematosus.

DR. C. R. ANDERSON: I still believe the patient has lichen planus.

DR. KENDAL P. FROST: This patient has presented an interesting problem. I am not satisfied that she has lichen planus. I agree with Dr. Anderson that there is a rather pronounced general reaction for lichen planus; yet I should expect lupus erythematosus of this distribution and type to produce a considerably greater systemic reaction than she shows. The lesions have cleared materially in the past few months, and I believe that the bismuth preparation and the mer-

cury which she has received have been factors in that improvement. However, I do not feel that metallic therapy of this type is specific or that any conclusions as to diagnosis can be drawn from the reactions to it. Brocq in his textbook emphasized eruptions which have characteristics of the two diseases. To these eruptions he applied the term "faits de passage," which I suppose can be well translated as "transitional types." Probably the condition in this case belongs in this group. I am inclined to feel that it tends more toward lichen planus than toward lupus erythematosus.

Tuberculosis Verrucosa Cutis. Presented by DR. NELSON PAUL ANDERSON.

C. G., a white man aged 29, was presented before this society in the early part of 1937. He is presented again to show the excellent result obtained by wide excision of the lesion by cautery. The wound was allowed to heal by granulation, and the cosmetic and functional results are excellent. Photographs show the condition before treatment and the size of the mass removed. The histologic report showed tuberculosis cutis.

DISCUSSION

DR. SAUL S. ROBINSON: I recently had the opportunity of treating a like condition by excision. The response was so satisfactory that I believe that is the better treatment.

DR. H. C. L. LINDSAY: I believe that if a primary infection of tuberculosis of the skin is discovered it is better to excise the lesion and so obtain a quick result. Cure can be effected in a few days by cutting, whereas by other methods it may take weeks or months.

DR. SAMUEL AYRES JR.: I think the therapeutic result is good. The choice is between excision and curettage under local anesthesia.

Toilet Seat Dermatitis. Presented by DR. NELSON PAUL ANDERSON.

V. H., a white girl aged 11 years, was seen eight weeks ago at the Santa Rita Clinic. She had an eruption on that area of the buttocks which comes in contact with the toilet seat. This eruption was more marked on one side than on the other. On questioning the mother, I found that the toilet seat had more of the mahogany stain coming through this side than the other side. The eruption had been occurring intermittently for four years, and it was learned that the toilet seat in the previous home of the family had been mahogany stained. I thought the condition was interesting as an unusual type of dermatitis due to an external irritant.

A Case for Diagnosis (Nevus or Tumor). Presented by DR. SAMUEL AYRES JR. and DR. CLEMENT COUNTER, Long Beach, Calif. (by invitation).

S. D., a white girl aged 5 years, presents two anomalies: (1) a diffuse swelling of the face associated with hemangioma and (2) hypertrichosis, which the mother says has been present since the age of 6 months. The latter condition would suggest some endocrine dysfunction.

DISCUSSION

DR. CLEMENT COUNTER, Long Beach, Calif. (by invitation): The child was brought in because of the angioma of the upper eyelid and the marked enlargement of the left cheek, the forehead and the side of the upper eyelid. I think the hypertrichosis must have something to do with the angiomatous lesion, but just how much is a question.

DR. KENDAL P. FROST: I suggest a diagnosis of hemolymphangioma.

DR. WILLIAM H. GOECKERMAN: A hemolymphangioma extending down to that area may explain all the changes, including the swelling. Further study, including a roentgen examination, may reveal a lesion much larger than would appear on the surface.

DR. L. F. X. WILHELM: I agree with the last two diagnoses. I think there is more hemangiomatous tissue under these areas and possibly in the lesions on the lids.

DR. H. C. LINDSAY: It would be advisable to take a roentgenogram. The antrum may be filled. The condition may be sarcoma.

DR. SAMUEL AYRES JR.: I agree with the various remarks that have been made. As far as the treatment is concerned, after investigation such as Dr. Lindsay has suggested, I think that exposure to filtered radiation would be advisable, but it is questionable how much relief may be obtained.

A Case for Diagnosis (Tinea Capitis? Alopecia Areata?). Presented by DR. F. I. BALL and DR. JOHN D. ROGERS (by invitation).

W. G., a Mexican boy aged 16, noticed a bald spot about 1 inch (2.5 cm.) in diameter on the left side of the neck one year ago. Later, other bald areas appeared, spread peripherally and were somewhat pruritic. Some of the areas show broken-off hairs which are easily epilated. None of the areas have been rough or scaly. Cultures were made on Sabouraud's medium, but the results were not conclusive. The treatment consisted of applications of 3.5 per cent solution of tincture of iodine twice daily.

DISCUSSION

DR. L. F. X. WILHELM: I think this case is one of alopecia areata.

(Drs. William H. Goeckerman, Kendal P. Frost and Saul S. Robinson agreed with this diagnosis.)

DR. SAMUEL AYRES JR.: I think it is one of tinea capitis. There are certainly broken hairs all over the affected areas, and the patient has some lesions on the neck which would not fit in with the diagnosis of alopecia areata.

DR. H. C. L. LINDSAY: I do not think the condition is alopecia areata, which never shows inflammatory lesions. This boy has a spot about the size of a half-dollar, which exhibits inflammation and scaling. There seems to be some hair all over the patch. I should not like to make a definite diagnosis until further study has been made.

DR. F. I. BALL: I do not think this condition is alopecia areata. I examined the slide, which showed mycelia and spores. The interesting feature is that there are no lesions typical of tinea.

Tuberculosis Cutis. Presented by DR. PAUL D. FOSTER.

D. N., a white American girl aged 12, was presented before this society at the meeting in January 1937 (ARCH. DERMAT. & SYPH. **36**:875 [Oct.] 1937). It was the opinion of the members at that time that the lesions which she had on the cheeks, the chest and the extremities were tuberculous. The histologic report by Dr. Nelson Paul Anderson showed tuberculosis. At that time several suggestions were made in regard to treatment. Solid carbon dioxide was used on one area and radium on several areas, and a series of roentgen treatments were given on all the areas. Twenty injections of 50 mg. of sodium gold thiosulfate were given. She has been given a preparation of liver, iron and vitamin B in capsules, viosterol and vitamins A, B, D and G. A salt-free diet has been adhered to, and adequate rest has been advised. In spite of the treatment, the condition has become worse. I am open to suggestions for treatment.

DISCUSSION

DR. H. C. L. LINDSAY: I should expect a patient with tuberculosis of such extent to be in poor health. If the patient has tuberculosis, the treatment could hardly be improved on.

DR. SAUL S. ROBINSON: I agree with the diagnosis of lupus vulgaris, and I believe the condition does best if the patient is hospitalized and put on a strict

salt-free diet. Sauerbruch reported success in the use of generalized ultraviolet irradiation. Hospitalization is necessary for the maintenance of rigidity in treatment.

DR. WILLIAM H. GOECKERMAN: What type of cutaneous tuberculosis could be present? I could not visualize any of the accepted forms of tuberculosis or tuberculid. I should favor a diagnosis of one of the papular diseases, such as lichen albus, lichen sclerosus or Czillag's disease.

DR. PAUL D. FOSTER: The diagnosis was made on the histologic picture rather than on clinical grounds. Sections from two lesions were studied, and I was satisfied that the condition was a form of tuberculosis.

Mycosis Fungoides. Presented by DRS. STANLEY O. CHAMBERS, STANLEY C. ANDERSON and M. N. ROSENBERG.

S. A., a man aged 58, is presented because of atrophic pigmented telangiectatic areas, in addition to typical tumor-like ulcerated nodules of mycosis fungoides. Dr. E. A. Oliver, of Chicago, saw this patient in 1932, at which time he made a diagnosis of poikiloderma atrophicans vasculare.

DISCUSSION

DR. WILLIAM H. GOECKERMAN: I agree with the diagnosis of mycosis fungoides. It is impossible to make any dogmatic statements in regard to poikiloderma atrophicans vasculare, because a multitude of cutaneous lesions have in recent years been included under this term. I think the original case which Dr. Jacobi presented had a striking and distinctive picture, and if his term is going to be used it should be used for that picture. I believe I have observed two cases in which that classic picture was present. I have observed many other cases which were designated as instances of that disease, but in which the picture was different from Jacobi's picture. When I visited Jadassohn's clinic some years ago, he showed one classic case, and I observed one other at the Mayo Clinic. In all other cases presented as instances of the disease when I was present, the picture did not correspond with the original description. Poikiloderma may be merely a variant of a group of diseases, but I am not inclined to think so. I saw my first patient with poikiloderma about fifteen years ago, and she still had the lesions ten years later. Her general health had remained good.

DR. MAX J. WOLFF: Dr. Oliver reported a case in the ARCHIVES (**33**:267 [Feb.] 1936) which he had had under observation for three years. He presented this case as one of typical Jacobi's disease.

DR. SAUL S. ROBINSON: I agree with the diagnosis of mycosis fungoides.

DR. H. C. L. LINDSAY: Most patients with mycosis live a comparatively short time. Patients with poikiloderma atrophicans vasculare whom I have seen are still alive, many of them after ten years. Patients with typical poikiloderma atrophicans vasculare look as if they had been burned by roentgen rays. As soon as one says anything dogmatic about this disease a controversy starts. Dr. Fred Wise (Lymphadenosis Cutis Universalis Associated with Generalized Erythrodermia and Atrophy of the Skin, *J. Cutan. Dis.* **35**:669 [Oct.] 1917) wrote: "In mycosis fungoides true atrophy of the skin with anetodermia or cigarette paper wrinkling is not known to occur, even in the end stages of the malady." Such an observation is helpful in making a diagnosis.

DR. M. N. ROSENBERG (by invitation): In this case there were two types of lesions. Some were atrophic, so-called poikiloderma; others presented a much more firm, hard, fibrous type of scar. Histologic sections tend to prove the scar was of the atrophic type.

Acne Vulgaris (with Keloids in Scars). Presented by DR. H. C. L. LINDSAY.

Rosacea and Peculiar Pigmentation of the Hands. Presented by DR. NELSON PAUL ANDERSON.

MANHATTAN DERMATOLOGIC SOCIETY

ANDREW J. GILMOUR, M.D., *President*

Dec. 14, 1937

ANTHONY C. CIPOLLARO, M.D., *Secretary*

Granuloma Annulare. Presented by DR. DAVID BLOOM.

C. M., a girl aged 11 years, has had a generalized eruption for the past two years on the extensor and the flexor surface of the lower extremities, the dorsa of the hands, the hips and the middle part of the back. Her family history revealed that her father had tuberculosis of the carpal bone at the age of 5 years and that a cousin had arrested pulmonary tuberculosis. The patient was in close contact with this cousin about four years ago, having slept with her from time to time.

The eruption, which has receded in the last four months, is located now on the flexor surfaces of the thighs, the knees, the ankles, the elbows and the forearms. It consists of discrete and confluent round, dime-sized and larger, slightly elevated somewhat violaceous lesions, with a distinct border of pinhead-sized papules. There are no subjective symptoms.

The microscopic examination of one of the lesions on the flexor surface of the right thigh revealed in the middle and the lower part of the corium mostly well defined round or elongated collections of epithelioid cells, lymphocytes and spindle cells, many of which were situated near and around blood vessels and hair follicles. No necrosis of the collagenous tissue was noted in a section stained with eosin and hematoxylin.

The general examination showed nothing abnormal. A roentgenogram of the lungs did not show any abnormality. The Wassermann reaction was negative. The Mantoux test with 0.1 mg. of tuberculin gave a positive reaction.

Lupus Erythematosus (Acutus, Disseminatus). Presented by DR. GEORGE M. LEWIS.

F. L., a nurse aged 32, was first observed in March 1937, when she stated that an eruption had first appeared on her cheeks five years before. It spread to the nose and was treated as eczema. Two years ago lesions began to appear on the hands and the arms. The eruption consisted of bright red scaly plaques, and the affected skin was thickened. Lesions of this character were present on the face, the fingers and the arms, and the buccal mucosa was the site of erythematous scaly lesions. The condition was determined to be acute disseminated lupus erythematosus. The patient was studied in the New York Hospital. Dr. William R. Williams found the patient to be in good physical health, and in particular her heart was considered normal. There was no elevation of temperature above the normal during her stay. A section of skin from a typical lesion revealed the histologic picture of lupus erythematosus. Studies of the blood showed no changes from the normal except for leukopenia (from 4,200 to 6,400 white blood cells). Examination of the stool and repeated examinations of the urine showed no abnormality. Therapy with a bismuth preparation was started, and twenty-six injections were given from March to July 1937, when she was greatly improved. Treatment was suspended during the summer months, which she spent in Canada. She rested during this time and kept out of the sun. In October, when she returned, gold therapy was started, and doses of 10, 10 and 15 mg. of sodium gold thiosulfate were given in successive weeks. After the third injection of gold salt on Nov. 4, 1937, an acute widespread erythematous eruption appeared. This has not yet entirely disappeared. Therapy with liver

extract intramuscularly apparently assisted in the disappearance of the toxic eruption. The original lesions appeared less noticeable than before, and the patient seemed slightly improved physically. The white blood cell count today was 4,200.

DISCUSSION

DR. MAX SCHEER: The lesions on the finger tips are rather erythematous. To me the condition looks like disseminated lupus erythematosus, and it may well be that the entire eruption is that rather than gold dermatitis.

DR. ISADORE ROSEN: In view of the fact that the patient improved so remarkably under bismuth therapy, I wonder why Dr. Lewis decided to give a gold preparation instead. I should like to ask whether the patient still had active lesions when she returned in the fall. From the history, I understand that she had about twenty-six injections of the bismuth preparation, which was adequate treatment. In treatment with bismuth I feel that the bad results or the lack of response to therapy is due to the fact that the medication is stopped too soon. In the clinic the treatment is given in courses: a course of twelve injections is followed by a rest period of six or eight weeks, after which the procedure is repeated. At least three courses a year are given. I find that the only cases in which treatment with a bismuth preparation is not successful are those in which insufficient therapy is given. I followed a series of 8 or 10 cases of active lupus erythematosus in which this form of treatment was satisfactory.

It is difficult to make a clinical diagnosis in this case. I have seen gold eruptions closely resemble lichen planus or lupus erythematosus. It is difficult to make a differential diagnosis clinically.

DR. DAVID BLOOM: I have learned to be cautious in administering gold preparations in cases in which there are numerous lesions of several weeks' duration on the face, for again and again I have seen exacerbations after minimal doses of a gold preparation had been given intravenously. In a boy of 18 with disseminated lesions of several weeks' duration on the face an exacerbation of the eruption developed after the administration of two doses of sodium gold thiosulfate, one of 5 mg. and the other of 10 mg., at weekly intervals. Lesions spread to the upper extremities; acute disseminated lupus erythematosus developed, and the patient died. In cases of disseminated lesions on the face it is advisable to start with injections of a bismuth preparation and observe closely the course of the eruption before administering a gold preparation. I feel that a small amount of gold may cause the whole process to flare up and produce acute disseminated lupus erythematosus.

DR. MIHRAN B. PAROUNAGIAN: I am inclined to favor the diagnosis of disseminated lupus erythematosus rather than that of gold dermatitis.

DR. GEORGE C. ANDREWS: I should like to ask whether this patient had disseminated lesions on the face of short duration or the chronic discoid type of lesions when treatment was started.

DR. MAURICE COSTELLO (by invitation): Did this patient have leukopenia before she was given the gold preparation? I have found that the sedimentation rate of the blood in cases of this type is invariably rapid and of prognostic importance.

DR. PAUL E. BECHET: In deciding whether to use gold preparations in disseminate lupus erythematosus, I think one should differentiate between the disseminate discoid type, for which aurotherapy is indicated, and the acute type resembling erythema multiforme, for which such therapy is contraindicated.

DR. E. WILLIAM ABRAMOWITZ: I think Dr. Lewis would like to know whether this patient has gold dermatitis. It is difficult to answer this question. The lesions on the nose resemble lupus erythematosus, but those on other areas look more like an exfoliating type of dermatitis due to heavy metals. It would be unwise to give an injection of a gold preparation to see if the condition gets worse, but a patch test may be of some help.

DR. ISADORE ROSEN: This patient presents oral lesions suggestive of lupus erythematosus. I wonder if Dr. Lewis observed them before instituting gold therapy.

DR. GEORGE M. LEWIS: In answer to Dr. Rosen, the patient had oral lesions when she was first examined. After twenty-six injections of a bismuth preparation it was felt that she should be given the benefit of aurotherapy. The administration of liver apparently produced improvement in her condition recently. In answer to Dr. Andrews, the lesions were disseminated but not of recent origin. Most of the lesions had been present for two years.

Recurrent Erythroderma. Presented by DR. MAX SCHEER.

A. M., a man aged 50, was first seen and treated on Oct. 5, 1937. At that time he said he had had an eruption on the legs for about three years. Roentgen treatments brought a certain amount of improvement. On two occasions, both within the previous few months, he had suffered from an acute widespread eruption followed by universal exfoliation. These attacks were of relatively short duration and under mild soothing treatment cleared within about one week.

Examination on Oct. 5, 1937, revealed an almost universal low grade erythroderma and a moist exudative and crusted dermatitis of the legs. The erythroderma improved rapidly, but the picture now became complicated by the development of furunculosis in both axillae. Roentgen treatment was administered for the furunculosis and produced astonishingly good results. The legs were treated with wet dressings of solution of aluminum acetate-tannic acid solution, 1 per cent silver nitrate, pastes and lotions, without improvement. About four weeks after the erythroderma cleared, the skin of the entire body again became erythematous and this time somewhat thickened. Within the last two weeks there has been more infiltration of the skin in some areas, notably the arms and the thighs, than at any time previously.

The patient's general physical condition is good, and no focus of infection has been found.

It has never been determined whether or not there is any relation between the eczema of the legs and the erythroderma of the body. No microscopic examination has been made as yet, since the necessity for histologic study only recently became obvious.

NOTE.—After presentation, this patient was hospitalized for a short time and his skin improved greatly. Studies of the blood showed no abnormality. The Wassermann and the Kahn test were negative, and the urine was normal. The pathologist could not make a definite diagnosis on the specimen removed from an infiltrated area on the back. His report stated that the changes in the epidermis suggested psoriasis and those in the cutis an acute toxic process.

Favus of the Scalp and the Toe Nail. Presented by DR. GEORGE M. LEWIS.

M. B., a single woman aged 28, a bookkeeper, first entered the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital four weeks ago, for advice concerning an area of alopecia on her scalp. She was born in the United States; her parents came from Poland. She stated that the bald spot had been present since childhood.

She has an area of almost total alopecia about the size of a quarter in the left parietal region. The outline of the patch is irregular. The surface of the skin is shiny and appears atrophic.

The left thumb nail has been affected for eight or ten years. At present the nail substance appears normal but is hypertrophic. The condition of the right great toe nail was first noticed four or five years ago. This nail is yellow, friable and dull and shows subungual hyperkeratosis. Examinations for fungi of material from the scalp and the finger nail gave negative results, but cultures from the toe nail revealed Achorion schoenleinii.

DISCUSSION

DR. PAUL E. BECHET: The clinical appearance of the lesions does not suggest favus. They could well be diagnosed as folliculitis decalvans. The correct diagnosis rests entirely on the microscopic picture and proves the necessity for microscopic study of atypical follicular dermatoses of the scalp.

DR. ANDREW J. GILMOUR: I noticed a yellowish coloration under the toe nail. That is almost the same color that appears in cases of active favus of the scalp.

DR. MIHRAN B. PAROUNAGIAN: I agree with the diagnosis and compliment Dr. Lewis for recognizing such a rare disease in this country. During my service at the Gouverneur Hospital, I saw this condition in a number of cases; in some it was of foreign origin and in others it had developed in a child born here of foreign parents. No doubt Dr. Abramowitz sees the condition in his service there.

DR. PAUL E. BECHET: At the meeting of the Atlantic Dermatological Conference in Philadelphia last Saturday, 2 sisters with favus were presented. Other members of the family were also affected. They were all American born.

DR. HOWARD FOX: Whereas ringworm of the scalp quickly runs through a family of children, favus may be present in only 1 or 2 members of a large family. The 2 patients mentioned by Dr. Bechet, who were presented at the recent clinic in Philadelphia, were members of a family of 7 children, every one of whom had favus.

DR. MAX SCHEER: The question of spreading the infection to other members of the family was brought up. Adults are much less susceptible than children, and it is unusual for an infection to occur in an adult. Generally the favus that adults have has probably been contracted in and persisted since childhood. I know of a doctor's wife who has had favus since childhood. The husband never acquired the infection, although he did not know it was favus until two years after they were married. The child likewise never contracted favus, because antiparasitic ointments were always used.

DR. HOWARD FOX: I agree with Dr. Scheer that favus when seen in adults nearly always has persisted since childhood. That favus may exist for many years is evident from a case mentioned by Sabouraud of a man aged 80 who had active manifestations of the disease.

DR. GEORGE M. LEWIS: This is the first time I have observed favus of a toe nail. Perhaps it would be detected if cultural diagnosis of all mycotic diseases was more generally practiced. It may be that favus is more prevalent in this country than was supposed. There are certain areas in different parts of the country where the condition is endemic. There are on record a number of instances of favus in American-born children and adults. There is a tendency to spontaneous cure of favus of the scalp, and that may occur in childhood or in adult life.

Recurrent Erysipelas. Presented by DR. GEORGE M. LEWIS.

CASE 1.—S. R., a housewife aged 63, the mother of R. S. (case 2), has had recurrent attacks of acute inflammation in the right foot and leg for fifteen years. There is usually one attack each year, which almost always comes in the summer.

The eruption consists of bright red, rapidly developing lesions with edema and is accompanied with constitutional symptoms. Between attacks there is enlargement of the entire leg below the knee. Cultures from the feet revealed Trichophyton gypseum. No streptococci were isolated from the throat or from the feet. Trichophytin tests showed negative reactions in twenty minutes, a 3 plus reaction in forty-eight hours and a 1 plus reaction after one week.

CASE 2.—R. S., a housewife aged 42, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital.

When she was 14 years of age (twenty-eight years ago), an eruption developed on her leg, which was diagnosed as erysipelas. There was not another attack until years later. Then for a period lesions appeared at irregular intervals. During the past eight years, with the exception of one year, she has had the same condition each summer. The attacks are similar, being ushered in with chills and high fever. The temperature is usually elevated to at least 105 F. The right foot and leg become reddened and swollen. The attack usually lasts a week or ten days. During the last attack sulfanilamide was used and apparently was effective. After the acute phase the leg showed edema of the ankle and enlargement of the entire leg when compared with the left leg. This gradually subsided, but the leg never entirely returned to normal. The leg is now in this inactive stage.

Her mother and aunt have had a similar condition. Fungi were demonstrated in scrapings from the feet, but cultures did not grow. Numerous strains of bacteria were isolated from the feet, including streptococci. Cultures from the throat showed no streptococci. The trichophytin test showed a 1 plus reaction in twenty minutes, a 3 plus reaction in forty-eight hours and a 1 plus reaction after one week.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: Years ago the condition in these cases used to be called elephantiasis nostras; now it is designated as solid edema. Williams and Traub showed that a similar condition may develop from a fungous infection.

DR. GEORGE M. LEWIS: Fungi were found on the interdigital webs of both patients, but this is probably of no significance. Streptococci were isolated from the webs of the younger patient. Cultures of material from their throats showed no streptococci.

A Case for Diagnosis (Melanoma? Pigmented Epithelioma?). Presented by DR. PAUL E. BECHET.

S. K., a man aged 39, states that he has had a lesion in the center of the left cheek since birth. It is oval and measures about 3 mm. in length and 1.5 mm. in width. The color varies from dark blue to intense black, and it has a raised rolled edge and a central depression. There is some surrounding induration. Hair is present on the lesion. The patient states that the lesion was flat up to puberty. After he began to shave, the lesion became elevated but did not increase in size. Three months previously the patient applied a patent corn remedy to the lesion, which formed a scab in its center; this came off after a few weeks and left the depression. Since that time, the patient states, the growth is larger. The patient states that he has had a cough and hemoptysis. A roentgenogram of the chest taken by the family physician showed an unchanging shadow in the right pulmonary field. The patient is losing weight and strength. His temperature ranges from normal to 101 F.

The Wassermann and the Kahn test were negative, and urinalysis showed no abnormality. A blood count showed 4,220,000 red blood cells, 10,000 white blood cells, 75 per cent polymorphonuclears, 24 per cent lymphocytes and 1 per cent eosinophils.

DISCUSSION

DR. J. FRANK FRASER: The diagnosis rests between pigmented epidermoid carcinoma and melanoma. I feel that the diagnosis will prove to be melanoma. Whether the lesion is a benign (pigmented mole) or a malignant melanoma cannot be determined from the gross appearance. Bleeding, ulceration and increase in size are the signs given in pathologic textbooks of malignant transformation in pigmented nevi. I suggest, provided there is no evidence (such as roentgenograms of the chest) that metastasis has already occurred, that the growth be widely

excised and that the presenter report the microscopic observations at a future meeting. If the sections show no malignant histologic changes, the prognosis is favorable. Even though the sections show signs of malignancy, the prognosis is not as bad as is generally believed. I have observed cases in which the lesions were histologically malignant and the patient was still living after three or four years. Such results, however, cannot be predicted, as metastasis may have taken place before removal of the primary tumor.

DR. MAX SCHEER: I think the patient's chest should be studied roentgenographically before the lesion is excised.

DR. PAUL E. BECHET: In my opinion, the clinical appearance of the lesion and the history strongly suggest the diagnosis of melanocarcinoma, as do the roentgenographic findings, the temperature, the failing strength, the loss of weight, the hemoptysis and a metastatic invasion of the lungs.

Morphea-Like Type of Basal Cell Epithelioma. Presented by DR. E. WILLIAM ABRAMOWITZ.

R. C., a woman aged 31, was first seen at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Dec. 1, 1937, with an eruption of three years' duration.

The patient presents a lesion on the right jaw, which she says started about three years ago as a small cyst. For the past year and a half there has been a slightly elevated white plaque, which has grown to the size of a 25 cent piece.

A microscopic examination showed characteristics of basal cell epithelioma. The Wassermann and the Kahn reaction were negative. Examination of the urine and a complete blood count showed no abnormality.

DISCUSSION

DR. GEORGE M. LEWIS: What method of therapy will Dr. Abramowitz employ in this case?

DR. E. WILLIAM ABRAMOWITZ: I shall recommend operation by scalpel.

Vitiligo Improved by Intravenous Injections of a Gold Preparation; Lichenoid Eruption Due to Gold Appearing Only on the Vitiliginous Areas. Presented by DR. MAURICE COSTELLO (by invitation).

F. B., a married woman aged 26, was first seen six months ago, when she presented widespread vitiligo of fourteen years' duration. It now covers half the body surface on both exposed and unexposed areas. Sodium gold thiosulfate was administered intravenously at weekly intervals, the dose beginning at 10 mg. and increasing gradually to 50 mg. Definite improvement in the vitiligo was noted in all areas after the fifth injection. After the twelfth injection a lichenoid eruption appeared on the arms and the legs. There was some regression of the lesions after discontinuance of the drug. One month later treatment was resumed, the patient receiving nine injections of 25 mg. of sodium gold thiosulfate intravenously. The eruption recurred about three weeks ago. It was limited to the vitiliginous patches, with a predilection for the flexor surfaces. Grayish dots varying in size from that of a pinpoint to that of a pinhead appeared on the right buccal mucosa. The depigmented areas assumed a yellowish tinge; the normal pigmented areas increased in color and extent, and the punctate perifollicular areas of pigmentation on the forearms and the legs coalesced. Moderate itching was present. In spite of the fact that the patient tried to avoid sunlight, she believes that she was more sensitive to sunlight than she had been previously. Areas of vitiligo on unexposed areas improved. She has 1 child, her first pregnancy having terminated in a miscarriage in the fifth month. Four Wassermann tests of the blood have been negative. A differential count of the blood showed

7 per cent eosinophils and 68 per cent hemoglobin. Histologic examination showed chronic inflammatory tissue, with some changes suggestive of lichen planus.

DISCUSSION

Dr. Howard Fox: Although I am not impressed with the value of gold salts in the treatment of vitiligo, I must admit that the photographs shown by Dr. Lindsay at the exhibit of the American Medical Association a few years ago certainly showed some improvement following treatment with such preparations. I know of no other method of treatment that has any permanent effect on vitiligo. Even the most intensive irradiation given at the Finsen Institute failed to produce lasting pigmentation of the patches.

Dr. Mihran B. Parounagian: I should like to mention my experience with 1 case of this type of vitiligo, although the involvement was not so extensive as that in this case.

I gave my patient sixty injections of triphal. In addition, a 10 per cent alcoholic solution of oil of bergamot was applied to the lesion, after which ultraviolet irradiation was given. Even though the patient thought the condition improved, I did not think so and discontinued treatment.

Dr. Paul E. Bechet: I am surprised that Dr. Costello obtained a favorable result from aurotherapy in a case of vitiligo, as my experience and that of many others have been entirely on the negative side. I have used it freely in a fairly large number of instances and have failed to see the slightest improvement. I have observed severe cutaneous reactions from the use of gold preparations in 2 cases of vitiligo. The cutaneous reactions from gold seemed greater in my cases of vitiligo than in those of lupus erythematosus.

Dr. George M. Lewis: Of 4 patients with vitiligo whom I have treated, 1 improved remarkably, but in the other 3 there was no therapeutic response.

Dr. George C. Andrews: I have been skeptical about the effects of gold preparations on vitiligo, and therefore I have not used such medication much. The condition changes spontaneously. That fact must be taken into consideration when results are reported. I should appreciate more details about this case—as to whether the patches became smaller when the improvement occurred, etc.

Dr. E. William Abramowitz: Clinically, the patient presents an eruption indistinguishable from lichen planus.

Dr. J. Frank Fraser: I should like to ask Dr. Costello whether there is a history of the ingestion of iodides in this case.

Dr. David Bloom: I have used gold preparations in about 6 cases of vitiligo at the Bellevue Hospital and have seen no improvement. In 1 case in private practice in which treatment with injections of a gold preparation and ultraviolet irradiation was employed, I observed the appearance of pigmented spots in the vitiliginous areas, but the result was not satisfactory. Regarding dermatitis following the administration of a gold preparation, I have observed such a manifestation in only 1 case among the many in which the treatment was used. In the present case a generalized lichenoid dermatitis has developed, followed by marked pigmentation lasting for a long time. This patient received 50 mg. doses of a gold preparation. The usual dose administered now does not exceed that.

Dr. Maurice Costello (by invitation): The patient applied at the clinic of the Bellevue Hospital for treatment of this condition, which has progressively increased since she was 12 years of age. I had never observed a case in which vitiligo improved during gold therapy. As I was prepared to see no change, I was surprised at the fairly rapid disappearance of many of the vitiliginous areas. There was no history of ingestion of other drugs. The patient stated that she intentionally avoided sunlight, but when casually exposed during the summer months her skin was more sensitive than ever to sunlight. Since a drug containing gold is photosensitizing, the question as to whether it should be given during the summer months in cases of lupus erythematosus is introduced.

Tuberculosis Cutis. Presented by Dr. Ludwig Oulmann.

A. B., a man aged 58, has been under treatment for pulmonary tuberculosis for the past five years. Three years ago his ring finger was removed because of osteomyelitis tuberculosa of the right hand. Shortly afterward, a verrucous lesion developed on the index finger of the same hand and extended over the dorsum of the three phalanges. The diagnosis at that time was tuberculosis verrucosa cutis. Roentgen and ultraviolet irradiation, electrocoagulation and a salt-free diet produced clearing, and the finger was normal for two years. Then the skin became violaceous and slightly swollen. The lesion increased in size. Now all three phalanges are affected in almost their entire circumference. There are no verrucosities and no apple jelly nodules.

DISCUSSION

Dr. Maurice Costello (by invitation): I was in Saranac Lake, N. Y., for six years, and during that time I never observed tuberculosis of the skin. This has been the experience of physicians who have practiced there for years. Tuberculosis of the skin accompanying active pulmonary tuberculosis is rare in the white race.

Spiradenoma (Adenomatosis of the Sweat Glands). Presented by Dr. J. Frank Fraser.

H. R., a man aged 54, has had an eruption for over ten years. The lesions consist of multiple, rounded growths varying in color from flesh to pink and in size from that of a lentil to that of a bean on the forehead and the scalp. The case is presented as a typical example of spiradenoma.

DISCUSSION

Dr. George C. Andrews: I have observed similar cases but none in which there were so many lesions.

Dr. J. Frank Fraser: Tumors of the sweat glands and ducts are closely related to the benign cystic epitheliomas. The histologic picture is highly characteristic. When the ducts are dilated to form cysts, the condition is known as syringocystadenoma or syringoma. In this case the tumor is an adenoma arising from the coil glands, and the microscopic picture is typical of spiradenoma.

Keratosis and Ulceration of the Tongue. Presented by Dr. J. Frank Fraser.

M. K., a man aged 68, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital two weeks ago with an ulcerated area on the left anterior lateral aspect of the tongue of five weeks' duration. A section of the lesion removed for microscopic study showed hyperkeratosis, acanthosis and a strong cellular exudate made up chiefly of plasma cells. There were no atypical cells or other histologic signs of cancer. The papillomatous appearance which the lesion now shows developed after the performance of the biopsy.

DISCUSSION

Dr. George C. Andrews: I am not satisfied with the clinical or the histologic diagnosis. I should dislike to see this lesion treated by the simple method of desiccation, because I think the conditions is too important to justify taking any chances. A practitioner should know exactly what he is doing when he treats such a condition. It would be a good idea to have another microscopic examination done before treating it.

Dr. Howard Fox: Clinically, this man has a hazelnut-sized, extremely hard lump in the tongue which I think is an epithelioma.

DR. MIHRAN B. PAROUNAGIAN: As it appears tonight, the condition strongly impresses me clinically as being an epithelioma. The age of the patient and the distinctly elevated lesion on the dorsum of the tongue, accompanied with ragged teeth corresponding to the area, would lead me to that diagnosis. As to the short duration, the patient might have had the lesion much longer. I should urge suitable treatment without delay.

DR. GEORGE M. LEWIS: I felt the lesion and can corroborate the statement of Dr. Fox that it is stony hard. I suggest that another microscopic study be made to establish the diagnosis.

DR. J. FRANK FRAZER: The section excised was definitely not carcinoma. In regard to the suggestion that another biopsy be performed, the best plan, in my opinion (on account of the small size of the lesion), would be complete excision, followed by a microscopic study of serial sections.

Amyloidosis. Presented by DR. J. FRANK FRASER.

H. W., an American man aged 42, a peddler, was first seen at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Oct. 8, 1935, with a generalized eruption of two years' duration. The eruption consisted of multiple scratch marks on the trunk, the thighs and the legs, with pigmentation most marked on the buttocks and the legs. There is no history of asthma or hay fever in his immediate family. The Wassermann and the Kahn test and examination of the urine and the blood showed no abnormality. Patch tests with potassium iodide gave negative results. When the patient was first seen, two years ago, avian scabies was suspected. The patient owned a canary, and he was the only one in his family who had taken care of it for five years. Recently, after this diagnosis had been excluded by examination of the bird, the patient was presented at a staff conference, and some of the members thought the condition was dermatitis herpetiformis. One of the sections taken for microscopic examination a year ago showed a single vesicle in the upper part of the epidermis which contained coagulated serum and polymorphonuclear cells. I am presenting this case as an example of amyloidosis of the skin on the strength of Dr. Satenstein's observations with special stains for the detection of amyloid.

ANDREW J. GILMOUR, M.D., *Chairman*

Jan. 11, 1938

ANTHONY C. CIPOLLARO, M.D., *Secretary*

A Case for Diagnosis (Cutis Anserina?). Presented by DR. MAURICE COSTELLO.

L. D., a girl aged 3 months, of Italian-American parentage, has had an eruption since birth. It consists of sudden generalized elevations of the skin, which appear within twenty seconds or less after stroking the skin or extending the limbs. The entire affected area is blanched, resembles crepe paper and has an uneven surface on palpation. Umbilication of the follicular openings is present, suggesting the appearance of scars following superficial burns. The peculiar appearance of the skin lasts from a few seconds to several minutes. It occurs many times during the day. Between attacks the skin appears normal. There are no objective signs of itching, and the child is in good general health. Another child, aged 2 years, is normal. There is no familial history of vascular disturbance.

DISCUSSION

DR. MAURICE COSTELLO: I have never seen a similar eruption. I wonder just how this should be classified. Should it be placed in the group of cutis anserina? The condition has not improved.

Angiofibromas in a Mongolian Idiot, Simulating Recklinghausen's Disease. Presented by DR. MAURICE COSTELLO.

R. D., a boy aged 11 years, is the fifth and last child in his family. His mother was 40 years of age when he was born. His lips are fissured, and his tongue is large, flabby and deeply furrowed. He is brachycephalic. His eyelids show signs of chronic blepharitis, and epicanthus is present. His ears are pitcher shaped.

On his scalp, face, neck and chest are about thirty elevated, globular, smooth, purplish red, semisolid nodules, varying in size from that of a split pea to that of a hazelnut. These lesions do not bleed except when traumatized. On the inner aspect of the right thigh there is a reticulated, pigmented area measuring 2½ by ½ inches (6 by 1.3 cm.).

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: Because of the absence of café-au-lait spots, I am inclined to class this case among those of generalized angiomatosis.

A Case for Diagnosis (Eczema?). Presented by DR. GEORGE M. LEWIS.

M. B., a boy aged 6 years, has had an eruption on his toes and his right middle finger for the past six months. His father was said to have had a similar condition, which had responded to treatment. Examination showed an acute inflammatory condition affecting the toes and the right middle finger. Microscopic and cultural studies of material from the feet, the toes and the finger failed to reveal fungi. The reactions to trichophytin and to oidiomycin were negative. The case is presented as of a not uncommon type in which the diagnosis of fungous infection is probable but in which an acute inflammation may mask the real condition or in which there is eczema unrelated to fungi.

DISCUSSION

DR. MIHRAN B. PAROUNAGIAN: Clinically the condition impressed me as probably mycotic, because of the changes in the nails. In spite of negative laboratory findings, I should be in favor of treating the condition as a fungous infection.

DR. ISADORE ROSEN: The clinical features resemble dermatophytosis. I should suggest a diagnosis of early acrodermatitis continua of Hallopeau on account of the undermined lesions, the resistance to therapy and the absence of fungi on microscopic examination.

DR. PAUL E. BECHET: The feet present typical dermatophytosis. Dr. Lewis states that two examinations of scrapings and cultures showed no fungi. I should suggest further examination for fungi before the diagnosis of dermatophytosis is discarded. Should further examinations give negative results I should seriously entertain Dr. Rosen's suggestion of possible acrodermatitis continua.

DR. GEORGE M. LEWIS: Microscopic and cultural studies to determine the presence of fungi are of the utmost importance in the management of suspected fungous infections. The negative reaction to trichophytin rules out an inflammatory fungous infection; if fungi are responsible for the primary disease, the inflammation is probably due to external applications.

DR. DAVID BLOOM: The marked subungual keratosis of two toe nails, together with the other clinical findings, suggests pustular psoriasis.

DR. MAX SCHEER: I should like to ask Dr. Lewis if he considered the possibility of this being dermatitis from the lining of the shoe or the socks.

DR. E. WILLIAM ABRAMOWITZ: I have had several such cases, and they were all in youngsters of this age. Some of the patients were examined by Dr. Lewis,

and they did not show any fungi. I believe that these children have something allied to acrodermatitis continua and can be treated only with solution of boric acid or boric acid ointment. If this condition developed in an adult and the question of a definite diagnosis came up, I should have to base my opinion on what was found. If tinea could not be found and contact agents were excluded, I should simply say that the condition was dermatitis from an unknown cause.

DR. GEORGE M. LEWIS: If a reliable person carries out the examinations for fungi and if a number of examinations are made at suitable intervals, the results should be fairly conclusive. Of course one can never entirely exclude the possibility of a fungous infection because of negative reports. The subject is of the utmost importance, particularly in cases involving compensation.

Blue Nevus. Presented by DR. ANDREW J. GILMOUR.

V. A., a housewife aged 32, born in the United States, states that early last summer, while she was bathing, she noticed a deep blue spot on the inner side of the middle third of her left arm. This spot has not changed in size and has caused no symptoms. There is no history of trauma near the nevus.

Examination shows a deep blue papule a little less than ¼ inch (0.6 cm.) in diameter, which is slightly raised. There is no sign of inflammation. Careful examination does not show any small pigmented dots around the lesion. Examination of the blood showed no abnormality.

This patient is presented for suggestions as to treatment and prognosis.

DISCUSSION

DR. ANTHONY C. CIPOLLARO: I think that many pigmented nevi have been treated unnecessarily radically. There are many of these lesions, and only rarely does one become malignant. They change only as a result of trauma. I should excise this lesion if it has been growing or showing other signs of activity; otherwise I should let it alone.

DR. MIHRAN B. PAROUNAGIAN: If this patient were much older, would the condition be regarded as malignant?

DR. DAVID BLOOM: I should like to know how to differentiate clinically between a melanoma which is malignant and one which is benign.

DR. J. FRANK FRASER: I recall a case in which generalized metastases were found at necropsy without any apparent change in what was apparently the primary lesion. In other words, it is possible to have malignant spread from a nevus which grossly does not show any indication of malignant transformation. To quote from Dr. Boyd: "The gross changes that indicate malignant transformation in nevi are hemorrhage, ulceration and growth." As the presence of the lesion is objectionable to the patient, I see no harm in following the suggestion that it be surgically removed. It will be interesting to see whether the histologic picture in this case shows the structure of blue nevus.

DR. GEORGE M. LEWIS: I suggest that the lesion be excised, since some type of treatment will probably be undertaken in the future. It is better to have a good surgeon employ wide excision than to have some inexperienced operator apply meddlesome therapy.

DR. E. WILLIAM ABRAMOWITZ: The actual clinical feature that must be used as a criterion is the color. I agree with the diagnosis of blue nevus, but I should still have a trembling hand in removing this, knowing that the color in itself is insufficient to distinguish blue nevus from melanoma.

DR. ANDREW J. GILMOUR: A man came to me with a nevus on the right cheek that resembled this one. There were small blue dots around the original lesion. Because of these dots I asked him to see another physician and to report to me. Instead, he was operated on by some one unknown to me. First the glands near the parotid gland were excised, and later the glands near the clavicle of the same side. The patient died in about six months.

Erythema Toxicum, Confined to the Left Lower Extremity. Presented by Dr. Maurice Costello.

D. N., a woman aged 65, had a fractured hip in 1936. She was in the hospital for three months. A silver pin was used to fix the fractured ends of the bone. The present eruption, which is confined to the antero-external aspect of the left thigh and leg, appeared as small red spots three weeks ago. These lesions, which were discrete from the beginning, became larger and coalesced in several places. The eruption consists of oval and round superficial lesions half the size of a dime, with narrow red borders and pale centers, in the middle of which are hemorrhagic puncta. The patient was questioned about bedbugs and said that she had never seen them in her home. She states that she has taken no medicines or laxatives of any kind. The only external medication was the application of white petrolatum and of tincture of iodine to a patch of eczema on the lower part of the left leg two weeks after the eruption appeared.

The patient has no subjective symptoms other than pain, which is always present in this extremity. A semicircular operative scar is located on the upper external aspect of the affected thigh.

DISCUSSION

Dr. J. Frank Fraser: I agree with the diagnosis. In regard to the unilateral distribution of the eruption, I believe that this can be explained by the fact that the patient has had a fracture of and operation on the femur and that there is less resistance on that side. In regard to the etiology, I suggest study of the patient's history and the exclusion of bacterial origin by careful search for foci of infection.

Dr. David Bloom: I observed this patient a few times, and I am convinced that the diagnosis as presented is correct. The central puncta, which are the result of tiny vesicles, made the presenter question the patient as to bites by insects. I feel that the unilateral localization of the eruption is due to the lessened resistance of this extremity.

Dr. E. William Abramowitz: It is interesting in this case that the patient had a preliminary lesion. The iodine coloration has faded now. She may have applied something else. I am inclined toward the diagnosis of erythema multiforme with the iris type of lesions.

Dr. George M. Lewis: The superficial, erythematous, scaly, rounded lesions of unilateral distribution favor the diagnosis of tinea circinata, and there are a few small vesicles. The injured hip may predispose to the development of a fungous eruption. I suggest repeated examinations for fungi.

Dr. Maurice Costello: Examination for fungi was not done, as I considered the eruption to be typical toxic erythema, with the operative intervention and the disturbance of circulation producing a locus minoris resistentiae.

Acne Indurata, with Neurotic Excoriations and Hypertrophic Scars. Presented by Dr. Paul E. Bechet.

M. B., a woman aged 24, has had moderate acne indurata on the face, the chest, the upper part of the back and the arms. A history of "picking" can be elicited. The patient presents a moderate discrete acne of the mild indurated type, mostly on the face. Scattered over the face, the upper parts of the shoulders, the chest and the arms are scars and excoriations varying in size from that of a pea to that of a lentil. The scars are elevated, indurated and keloid-like. Their color varies from pale red to porcelain white, depending on their age, and they are all in the most accessible regions. There are many fresh crusted lesions. Several of the crusts are composed of dried blood and serum. The patient evinces a tendency to hypertrophic scars, the scars of an old thyroidectomy being unusually prominent.

DISCUSSION

Dr. Isadore Rosen: I agree with the diagnosis of some form of neurotic excoriation, but I fail to see any clinical evidence of acne on the face. I believe

that these lesions are similar to those on the trunk and result in the formation of scars and keloids.

DR. MAURICE COSTELLO: I agree with Dr. Rosen that this patient has neurotic excoriations. No comedones are present; the areas involved are on accessible locations beyond the favorite sites for acne, and the pharyngeal reflex is absent.

DR. PAUL E. BECHET: There are indurated papules, pustules and comedones in typical locations for acne. There are excoriated, crusted lesions in the most accessible locations only. Some of them are so fresh that they are covered by dried blood. The patient is neurotic and gives a history of picking. It would seem most plausible to surmise that the patient first began to pick the actual lesions of acne and then, as the habit grew apace, picked on any inflammatory spot no matter how insignificant; this, together with a tendency for hypertrophic scarring or even true keloids to develop, has produced a most disfiguring condition.

Onychodystrophy and Atrophy of the Terminal Phalanges Caused by a Cervical Rib. Presented by DR. ANTHONY C. CIPOLLARO.

L. S., a white woman aged 25, was previously presented before this society on Oct. 11, 1937 (ARCH. DERMAT. & SYPH. **37**:530 [March] 1938). Since then the following data have been obtained:

Mycologic examination of clippings from the nails showed no fungi. Careful examination of the cutaneous surface failed to show evidence of either psoriasis or onychomycosis.

Roentgenograms of the left hand showed a moderate degree of absorption of lime salt, with slight atrophy of the terminal tufts of the thumb and the middle finger. Those of the cervical portion of the spine showed an articulated cervical rib on the left side of the seventh cervical vertebra. This articulated portion extended downward and forward about 1 inch and tapered toward the distal end. When the head was extended, the left radial pulse was temporarily obliterated. No sensory disturbances were found.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: I saw this patient with Dr. Cipollaro at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. I believe I suggested taking a roentgenogram to see if she had a cervical rib, because there was nothing else to account for the localization of this one-sided atrophy of a few fingers. I am glad to see this conjecture verified.

DR. MAURICE COSTELLO: In the course of several years I have studied many roentgenograms of the chest and have seen about six cervical ribs. They are usually bilateral, and in no case was the condition similar to this one. It is possible that the angle of the rudimentary rib is such as to cause pressure on the brachial plexus. I believe that it would be best to forego the difficult operation of excising this anomalous rib. Lateral and stereoscopic roentgenograms might reveal its angle of inclination.

DR. E. WILLIAM ABRAMOWITZ: Recently I read an article on cervical ribs in which it was stated that a few persons who have a cervical rib have no symptoms whatever. Only in cases in which there are symptoms is a search made for the anomaly. It is the pressure from the unnecessary rib that gives rise to all the trouble.

Supernumerary Auricles. Presented by DR. MAURICE COSTELLO (by invitation).

H. H., a man aged 58, has two accessory auricles on the right tragus. The larger one is pedunculated, and its clubbed end is the size of a bean, semisolid and covered by normal skin. A cartilaginous core can be palpated at the point where it arises from the skin. The other, below this, is the usual type of single supernumerary ear and is half the size of a pea. The patient's brother has a similar condition on the opposite ear.

DISCUSSION

DR. DAVID BLOOM: This condition is described in the literature as supernumerary tragi. It is a congenital malformation, easily understood when considered from the standpoint of embryonic development. The first case of this kind which I observed was in the obstetric ward of the Bellevue Hospital. At that time I was informed that the pediatricians encounter many such cases. Microscopic examination of one of these appendages revealed a cartilaginous core.

DR. MAURICE COSTELLO: In the case referred to by Dr. Bloom I excised one of the pedunculated accessory auricles. The histologic examination showed a central reticular cartilaginous core, subcutaneous cellular tissue and skin. This condition is frequently familial and associated with other developmental anomalies, such as extra nipples. Warner examined 50,000 school children and found accessory auricles in 35.

A Case for Diagnosis (Lymphoblastoma? Xanthoma?). Presented by DR. DAVID BLOOM.

J. H., a man aged 64, states that the present eruption developed about five months ago. He believes that the eruption on the neck and the back started about that time and the eruption on the extremities about three or four months ago.

The generalized eruption consists of different types of lesions. On both sides of the neck are brownish, yellowish or skin-colored pea-sized papules, slightly infiltrated and closely aggregated. The lesions on the nose are brownish, flat and barely infiltrated. On the ears are pea-sized raised infiltrated brownish papules. Similar papules are seen on the upper part of the back, and there are a few on the chest. On the elbows, the extensor surfaces of the forearms, the knees, the dorsa of the hands, some phalangeal joints, the extensor surfaces of the legs, the ankles and the buttocks there are markedly raised and infiltrated violaceous tumors, varying in size from that of a dime to that of a quarter and having a distinct brownish tinge, and a few flat infiltrated plaques.

The personal and the family history are of no importance. The patient seems to be in good general condition, and his complaint consists only of some discomfort when sitting down.

General examination does not show any abnormalities except inguinal glands of the size of a walnut, which are firm and not tender. There is no enlargement of the liver or the spleen. Roentgenograms of the lungs and the bones did not reveal any abnormality. Examination of the blood showed 100 per cent hemoglobin, 3,720,000 red cells and 6,200 leukocytes. The differential count showed 63 per cent polymorphonuclear leukocytes, 31 per cent lymphocytes and 6 per cent eosinophils. Examination of the urine showed no abnormality, and the Wassermann reaction was negative. The tuberculin test with a dilution of 1:10,000 gave a negative result and with a dilution of 1:1,000 a positive result. A chemical examination of the blood revealed 106 mg. of sugar and 32 mg. of nonprotein nitrogen per hundred cubic centimeters of blood. The contents of albumin and globulin, of total lipoids and of esters are within normal limits. The total cholesterol content is 260 mg. per hundred cubic centimeters (the maximum normal reading is 254 mg.). The amount of free esters is somewhat increased, being 117 mg., while the maximum normal figure is 89 mg. The lipid phosphorus content is within normal limits.

Histologic examination was made of a tumor-like lesion from the knee and of a papule from the neck, and the following comment was made by Dr. T. J. Riordan: "The former lesion showed the end-result or the subsiding part of an inflammatory process which caused a marked increase in the number of the capillary blood vessels, with thickened walls and fibrotic surrounding infiltration. Syphilis could be excluded. The section from the neck showed acanthosis (cut tangentially), with an underlying granulomatous corium showing profuse infiltration of small and large round cells, large oval cells, fibroblasts, occasional epithelioid cells and numerous eosinophils. The granulomatous appearance of the

latter section suggested mycosis fungoides or a similar lymphoblastoma as a remote possibility. The large reticulum cells suggested Hodgkin's disease. However, no definite diagnosis could be made from the sections."

DISCUSSION

DR. ISADORE ROSEN: From the clinical features, one would be inclined to place the condition in the lymphoblastoma group. Mycosis fungoides can be ruled out because of the uniformity of the lesions, the absence of a previously existing eruption or of eczematization and the mildness of the subjective symptoms.

DR. PAUL E. BECHET: In my opinion this is the most interesting case which has been presented tonight. It seems a pity that the histologic report throws so little light on the diagnosis, as it is extremely difficult to make a diagnosis on the clinical appearance of the lesions alone. Another puzzling feature is the patient's statement that the eruption has been present for only three weeks. Judging from its appearance, I should say that such a statement is bound to be fallacious, for none of the clinical possibilities is compatible with such a brief period of evolution, unless it be a drug eruption due to a halogen. Time and the uniformity of the lesions might favor that diagnosis. For obvious reasons, I should not consider either xanthoma or mycosis fungoides of the d'emblée type. The flat, sharply outlined, purplish red lesions on the heels are somewhat suggestive of Kaposi's sarcoma, but the rapid onset is against such a diagnosis; yet the condition may ultimately be found to be due to a low grade malignant type of general sarcomatosis.

DR. MAURICE COSTELLO: Because of the duration and the appearance of the lesions, I believe that this condition is erythema elevatum diutinum.

DR. E. WILLIAM ABRAMOWITZ: As long as there is no correlation between the clinical appearance and the pathologic picture in this case, I should like to ask what drugs this patient has been taking. Perhaps this condition may be a bromide or an iodide eruption.

DR. ANTHONY C. CIPOLLARO: Can the histologic studies rule out Spiegler-Fendt sarcoid? On examining the smaller lesions, I noted characteristics similar to those in a case under observation now at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. In that case several pieces of tissue were removed, and a diagnosis of Spiegler-Fendt sarcoid was made. I suggest that a few of these lesions be closely shielded and treated with roentgen rays, because the lymphoblastomas are radiosensitive.

DR. MIHRAN B. PAROUNAGIAN: The microscope will have to decide the diagnosis. I cannot reconcile the diagnosis of mycosis fungoides with the history. The duration (four or five months), the perfectly symmetrical eruption, the absence of itching and the elevation of the lesions are things that I think speak against that diagnosis. Dr. Abramowitz' suggestion of a drug eruption should be considered seriously.

DR. DAVID BLOOM: The diagnosis of xanthoma was made because of the yellowish brown lesions on the neck and the face. However, that diagnosis seems to be disproved by the microscopic picture. Both Drs. Riordan and Satenstein studied the slides, and both thought of the possibility of mycosis fungoides or some form of lymphoblastoma. Although clinically the condition does not look like mycosis fungoides, that is a possible diagnosis. The suggestion of Dr. Abramowitz as to a drug eruption is well taken, although the patient states that he has taken no drugs. Some of the material is being examined for the infiltration of fat, the result of which will be reported later.

Report on a Case for Diagnosis (Melanoma? Pigmented Epithelioma?).
Presented by DR. PAUL E. BECHET.

S. K., a man aged 39, was previously presented before this society on Dec. 14, 1937 (ARCH. DERMAT. & SYPH., this issue, p. 909). He had a melanotic lesion

in the center of the left cheek 1 inch (2.5 cm.) long and ¼ inch (0.6 cm.) wide, with a depressed center and a rolled indurated border. The patient was losing weight and strength and had bloody sputum. The clinic for patients with tumors reported that a roentgenogram of the chest revealed definite metastases and that under the circumstances a biopsy was not advisable.

CHICAGO DERMATOLOGICAL SOCIETY

OTTO H. FOERSTER, M.D., *President*

Dec. 15, 1937

H. RATTNER, M.D., *Secretary*

Permanent Pigmentation Following the Application of Ferrous Sulfate for the Treatment of Poison Ivy. Presented by DR. S. W. BECKER and DR. E. E. STENHOUSE (by invitation).

K. H., a woman aged 35, presents a deep brown pigmentation of the left cheek and the upper part of the left arm of four months' duration. Late in August 1937 the patient had an extensive oozing, vesicular eruption about the left cheek and the upper part of the left arm, resulting from contact with poison ivy. Calamine lotion produced no relief. At the suggestion of friends, wet dressings of a 4 per cent solution of ferrous sulfate were applied for four days. When the condition did not improve, a physician was consulted, and he advised wet dressings of potassium permanganate. The only other medication applied was a poison ivy lotion that contains lead acetate, gelsemium, phenol and hamamelis. The patient is not sure whether this was applied before or after the ferrous sulfate.

The discoloration was noted at the time the ferrous sulfate was applied. However, the patient believes that the pigmentation is slightly less intense now than it was at first.

The pigmented lesions are macular, well circumscribed and smooth and vary from punctate size to 4 mm. in diameter. They are found only at the sites of the original vesicles.

Histologic examination of a biopsy specimen taken from the arm showed the pigment to be deposited in the upper part of the corium in the chromatophores and lying free between the collagen bundles. Berlin blue showed a large amount of iron deposited in the upper part of the corium.

DISCUSSION

DR. THEODORE CORNBLEET: The precipitation of iron under such circumstances has been seen a number of times. Recently it has been shown that acetate and iron are prone to produce precipitation and form a tattoo, but perhaps some other combination besides iron and acetate could be guilty of causing such deposits. I think the lesson to be drawn from this is that only one agent should be used in treating such a condition. I observed a similar case in which a compound called amertan (5 per cent tannic acid and merthiolate 1:5,000 in a water-soluble jelly base) was used on a second degree burn after mercurochrome had been applied. The result was a permanent deposit which looked like a mercury precipitate. The discoloration cleared partially during the use of solid carbon dioxide, and for a while improvement continued after the treatment stopped. I have the feeling that in many cases the lesions will partially clear spontaneously. Iron precipitates may absorb slowly; after encapsulation, however, absorption slows or stops, leaving a residual permanent discoloration.

DR. S. W. BECKER: I appreciate Dr. Cornbleet's remarks. We are planning to do some intensive work to find what causes this condition. The lesions have

already faded to a certain extent. This is only the fourth month, and I think the patient will soon be able to use some preparation to cover up the discoloration. She has tried this, but the lesion on the arm is so intense that it is difficult to cover.

Pityriasis Lichenoides et Varioliformis Acuta. Presented by DR. S. W. BECKER and DR. M. E. OBERMAYER.

C. W., a white man aged 52, states that a generalized nonpruritic eruption suddenly developed one month ago. Examination showed a papular eruption, involving the flexor surfaces of the arms and the thighs, the palms, the soles, the groin and the buttocks. The lesions were fairly uniform in size, ranging from 0.5 to 1 cm. in diameter, slightly infiltrated and of a copper brown. Some of them showed fine scaling. The clinical impression was that of a papulosquamous secondary syphilid.

The past history was of no significance. The patient had consulted us two years previously for seborrheic eczema of the scalp and a dry dermatitis of the legs, which cleared promptly under treatment. He states that he has had no sexual contacts and that he has taken no drugs.

General examination showed no abnormality. The blood and differential count were normal, and the Wassermann and the Kahn reaction were repeatedly negative.

During treatment, which has consisted of application of erythema doses of ultraviolet radiation and of a mild ointment containing sulfur and salicylic acid, new crops of lesions, some of them varioliform, have developed, while other lesions have healed without leaving scars. Lately the face has become involved.

A biopsy specimen from a papular lesion on the right side of the chest showed the stratum corneum to be hyperkeratotic and parakeratotic but not thick. The stratum granulosum was absent over much of the section and thin in other places. The stratum mucosum was thin, edematous and in several places infiltrated with round cells. The cutis was edematous and showed a moderate perivascular infiltrate of round cells, largely limited to the subpapillary portion.

DISCUSSION

DR. F. E. SENEAR: From the clinical picture, in spite of the fact that the eruption has been present only a month, I feel that pityriasis lichenoides chronica (Juliusberg) would explain all that appears here. However, there are some lesions about the ankle which give a suggestion of greater acuteness than is found in the chronic type, and I think that if other lesions of that type have been observed elsewhere the condition may be on the borderline, showing transition from the Juliusberg type to the more acute variety. The general picture today, however, is that of pityriasis lichenoides chronica rather than of the Habermann type.

DR. M. E. OBERMAYER: Two factors made us feel justified in making the diagnosis of the acute type: (1) the few varioliform lesions which were present on the legs on one occasion and (2) the inflammatory reaction observed in the histologic specimen, which seemed to be more acute than is usually observed in the chronic form.

Following Gougerot's method, we have treated 2 patients with intravenous injections of a gold compound, but no clinical improvement resulted.

DR. OLIVER S. ORMSBY: I should suggest the use of ultraviolet quartz radiation from a lamp, which has been of much value in several cases under my observation.

DR. OTTO H. FOERSTER, Milwaukee: Ultraviolet radiation has been given, but new lesions continue to develop.

DR. CLARK W. FINNERUD: I observed 2 similar cases in Vienna in which Dr. Oppenheim cleared up the condition with injections of tuberculin. In these cases the condition was of the Juliusberg type.

Naevus Unius Lateris. Presented by Dr. David V. Omens (by invitation).

J. H., a Jewish girl aged 6 years, has had this nevus since birth. The mother has a large pigmented nevus involving the extensor surface of the left arm.

Examination shows a linear patchy verrucous brownish eruption involving the left side of the body—especially on the anterior surface and the left arm—and the anogenital area. Pruritus is the only subjective symptom. The mother presents a pigmented nevus involving the extensor surface of her left arm, which has been present since birth.

DISCUSSION

Dr. M. E. Obermayer: The interesting fact is the linear distribution in both patients. Even if the type of lesion differs—1 being an ichthyosiform nevus and the other macular—it is remarkable to see that the hereditary tendency in the development of nevi was sufficiently marked to produce a lesion with the same linear distribution in the mother and the daughter.

Dr. H. Rattner: With reference to birthmarks in general, I remember seeing the statement some time ago that birthmarks occur most often in the first child of an older mother. I thought the statement interesing and made a check at St. Vincent's Orphanage, where the mothers are younger than those ordinarily found in a group, and could not verify the statement at all.

A Case for Diagnosis (Nodular Neurodermatitis?). Presented by Dr. Theodore Cornbleet.

E. L., a white woman aged 26, had an eruption at the site of her present one about eight years ago. This was pruritic. Gradually the present lesions evolved out of the former ones. These are now thickened, dry, grouped nodules on the right labium majus and on the area immediately to the right of this, as far as the crease of the thigh. They are abruptly raised from the cutaneous surface, have smooth surfaces, feel like small keloids and are pruritic.

The lesions have become smaller under roentgen therapy, and the pruritus has decreased.

During the last several months there has been a scanty vaginal discharge, in which Trichomonas vaginalis has been found. There has been no vaginal discharge prior to the last few months.

The histologic examination showed a thick, adherent hyperkeratotic scale. The epidermis was thickened, and there was an irregular lengthening of the rete pegs. There was considerable intercellular edema and in one place an intra-epidermal vesicle. Except in this one area, the granular layer was continuous.

The corium was edematous; there was dilatation of the blood vessels, and about each vessel was a loose edematous mantle of lymphocytes, histiocytes and plasma cells. This infiltration was more marked in the upper part of the corium, but it did not extend up to the epidermis.

DISCUSSION

Dr. S. W. Becker: This picture is interesting. The unilateral distribution and the histologic picture of chronic inflammatory lichen corneus hypertrophicus suggest naevus unius lateris of prenatal type. The eruption is not definitely lichenified, is strictly unilateral and does not have the fading border of neurodermatitis.

Dr. M. H. Ebert: I think Dr. Becker's suggestion is a good one. However, from the histologic section and the clinical appearance of the lesions I was of the impression that the condition might be lichen corneus hypertrophicus, a variety of lichen simplex chronicus. In this disease the lesions are discrete and pruritic, and in the histologic sections spongiosis is an important feature, as in this case.

Dr. James H. Mitchell: I thought the lesions were rather smooth instead of keratotic.

DR. LESTER M. WIEDER, Milwaukee: The borders of two of the lesions were linear and formed acute angles. I suggest this lesion might be neurodermatitis developing at the site of old hypertrophic lichen planus.

DR. THEODORE CORNBLEET: My view of the genesis of these lesions is that the patient originally had herpes progenitalis that was pruritic and when scratched created nodular neurodermatitis. I do not see how Dr. Becker's suggestion can be substantiated. The lesions have subsided under roentgen therapy, and so has the pruritus; it would appear that if this condition were a nevus the lesions would not react in such a way. Furthermore, the lesions commenced rather late in life for a nevus of that kind. While nevi may make their appearance in late life, it is unusual.

DISCUSSION

DR. PAUL A. O'LEARY, Rochester, Minn.: My thoughts in this case are different from those that have been expressed thus far. It seems to me that the lesions are scars—possibly hypertrophic rather than keloidal scarring.

Pityriasis Rubra Pilaris. Presented by DR. E. A. OLIVER and DR. F. J. KENDRICK, Gary, Ind. (by invitation).

D. C., a boy aged 7 years, states that he had rather mild pharyngitis, lasting twenty-four hours, about six weeks ago. About two weeks following the sore throat, the present eruption began, appearing first on the palms.

There is now diffuse exfoliation of the palms and the soles and sharp, warty, follicular patches on the knees and the elbows. There are scaly patches at the edges of the auditory canals.

We have been unable to convince the health officer that the patient is not suffering from a postscarlatinal exfoliation.

This case resembles closely one shown by Drs. Finnerud and Tobin at a recent meeting (ARCH. DERMAT. & SYPH. **37**:709 [April] 1938). (Dr. Tobin's patient was present at this time.)

DISCUSSION

DR. JAMES H. MITCHELL: I discussed the other case at the other meeting. This boy's condition reminds me of that of a patient Dr. Ormsby and I observed at least twenty years ago. That patient had had a severe sore throat, and we thought of the possibility of pellagra, but not all the symptoms of that condition were present. These symptoms are manifestations of some toxic process.

DR. OLIVER S. ORMSBY: In the interim since observing the case described by Dr. Mitchell, I have observed several others, always involving children; in none of them did pityriasis rubra pilaris subsequently develop. In these cases palmar keratoderma followed erythema of the palms, which occurred coincidentally with general symptoms, i. e., angina and elevation of temperature. I have considered these cases as examples of toxic keratoderma which cleared up in a reasonable time. While the condition in these cases suggests pityriasis rubra pilaris, it is not that, and it is possible that this patient's condition will prove in time to belong in the toxic group.

DR. OTTO H. FOERSTER, Milwaukee: Would the absence of involvement of the scalp, which is so frequently affected in pityriasis rubra pilaris, help in the differentiation?

DR. CLARK W. FINNERUD: I believe these 2 cases, in spite of their similarity, possibly are instances of two entirely different diseases, although in both there is keratoderma of the palms, the soles, the fingers, the knees and the elbows. I should not be surprised if the first case presented today, that of the boy, proves to be an instance of keratoderma rather than of pityriasis rubra pilaris. I cannot help thinking, however, that the first one, which closely resembles one I showed a long time ago in which the diagnosis was proved, is an instance of true pityriasis rubra pilaris. The involvement of the scalp and the face is characteristic, although there are no follicular keratoses of the backs of the fingers, the neck and other areas commonly so involved.

DR. W. W. TOBIN (by invitation): I believe that the condition in this case is identical clinically with that in the one shown at the last meeting. However, this patient's disease is of only six weeks' duration and followed an infection of the upper part of the respiratory tract, while the disease in the other case was of two years' duration and there was no preceding infection.

A Case for Diagnosis (Nodular Eruption). Presented by DR. F. E. SENEAR.

J. K., a woman aged 33, states that a nodule developed on the left side of the forehead and a similar lesion on the left upper eyelid in May 1937. They were arciform nodules which were dull red and rather firm. A few acneform lesions were scattered over the cheeks. She states that about five years ago she had several lesions similar to the nodular ones now seen and that these persisted for several months.

The nodular lesions were not typical of any disease but suggested syphilis or sarcoid at that time. The serologic reaction was negative. After two treatments with roentgen rays the lesions disappeared in about three weeks. Four weeks later, however, a new nodule of similar character developed in the left malar region. This likewise persisted for several weeks. No scarring followed the involution of any of these nodules.

The patient was not seen again until two weeks ago, at which time a number of these nodules had developed on the cheeks, the chin and the submaxillary region. Some of these were similar to the lesions seen before, but others were papules the size of a large pea, with a whitish center suggestive of the presence of some pus. Many have coalesced to form agminated groups; others have enlarged by peripheral extension to form coin-sized plaques with a depressed center and a border consisting of reddish nodules with whitish centers. There was no history of ingestion of medicines, but the urine was not examined for iodides or bromides.

The histologic examination showed a moderate degree of intracellular and intercellular edema in the epidermis. There were narrow mantles of round cell infiltration around the blood vessels and a diffuse infiltration of lymphocytes, histiocytes and connective tissue cells throughout the corium. In one area there was much free blood in the corium.

DISCUSSION

DR. CLARK W. FINNERUD: I have observed several similar cases in which a transitory eruption appeared and lasted from a few weeks to a few months. The condition occurred usually in the summer. Lupus erythematosus is known to be transitory sometimes, until it becomes fixed, and in spite of the fact that one cannot make a definite diagnosis from this section, I feel that, rather than erythema elevatum diutinum, granuloma annulare, sarcoid or erythema perstans, which it sometimes resembles, the condition is lupus erythematosus. The histologic changes presented in these sections were not incompatible with the early changes in that disease.

DR. THEODORE CORNBLEET: I observed a patient who had had Duhring's disease for some time and in whom a similar lesion formed to the left of the nose. This disappeared within four days after one intravenous injection of iron cacodylate. The lesion was indurated and somewhat circinate and had all the characteristics of the one this patient shows.

DR. PAUL A. O'LEARY, Rochester, Minn.: In the differential diagnosis I considered, in addition to lupus erythematosus, erythema elevatum diutinum and the exanthema of leprosy. Although the lesions have been transient, it would seem advisable to search for the Hansen bacillus. I favor the diagnosis of erythema elevatum diutinum, because by exclusion the other diagnoses seem less probable.

DR. F. E. SENEAR: I considered lupus erythematosus and for the first three lesions I considered sarcoid and syphilis. In the picture today there is no suggestion of sarcoid. I did consider erythema elevatum diutinum and granuloma annulare.

A Case for Diagnosis (Blastomycosis?). Presented by DR. E. A. OLIVER, DR. F. J. KENDRICK, Gary, Ind. (by invitation) and DR. RALPH H. SCULL (by invitation).

E. P., a railroad laborer aged 34, born in Italy, presents a generalized eruption of four years' duration.

The eruption began as a small group of resistant papulopustules on the chin. It has gradually involved nearly all parts of the body. On the face and the extremities and to a lesser degree elsewhere are numerous rather sharply demarcated lesions, from the size of a dime to that of a dollar, which are indolent, indurated and more active at the border. Pus lies deep in the lesions, and there is a tendency for them to be polycyclic. There are some smooth scars.

The Wassermann test gave repeatedly negative results. Potassium hydroxide revealed no organisms.

The histologic examination showed no organisms, but structurally the picture was suggestive of squamous cell epithelioma.

About six or eight months ago the patient was treated by another doctor for syphilis, receiving a number of injections of neoarsphenamine, which produced no improvement.

DISCUSSION

DR. CLARK W. FINNERUD: The section presented is so poorly stained as to be worthless. Apparently neither the hematoxylin nor the eosin was working properly, and the section is far too thick. I feel that persistent search will result in demonstration of the blastomycetes.

DR. JAMES H. MITCHELL: I should not say the condition is blastomycosis, but clinically it has characteristics of that disease and failure to find the organisms is not against the diagnosis. There is pus, but the light and everything were against me in making the examination. I saved some of the material and will try to make cultures, although the ease of obtaining a culture in a case of blastomycosis varies tremendously. Sometimes I get positive cultures in every tube, and sometimes it takes nearly a hundred attempts before I actually get the organism.

DR. M. H. EBERT: I should like to ask whether the condition of the face is the result of the same type of eruption and is of the same duration as the lesions of the body. If that is the case, I should like to suggest that this man may be one whose resistance to ordinary pyogenic bacteria is low, the disease starting as a follicular infection on the face and, as his resistance lowered, spreading to other parts of the body.

DR. THEODORE CORNBLEET: I suggest that if the presenters have any further difficulty in isolating the organisms they administer a small amount of potassium iodide a few days prior to the search.

Epithelioma Tuberosum. Presented by DR. OLIVER S. ORMSBY and DR. W. W. TOBIN (by invitation).

S. D., a man aged 52, is presented because of an eruption on the face of four months' duration. He states that it began as a hard papule on the left cheek and that shortly thereafter other hard growths appeared about it. These have gradually enlarged. He states that for the past twenty-five years he has had scaly reddened areas about the face and that five years ago several of these were removed by roentgen therapy.

The patient has a senile skin, with many scattered senile keratoses on the face. On the left cheek, extending to the nose, are grouped nodular infiltrated bluish red lesions, from the size of a walnut to that of an egg, which are centrally ulcerated. There is a chain of painless discrete hard cervical glands on the left side.

The Wassermann test gave a negative result.

The histologic examination showed masses of epithelium arranged in columns, with moderate dyskeratosis, numerous mitotic figures and a perivascular infiltrate of lymphocytes and plasma cells.

Epithelioma Tuberosum. Presented by Dr. Oliver S. Ormsby and Dr. W. W. Tobin (by invitation).

M. M., a man aged 64, is presented because of an erption on the upper part of the left cheek of two months' duration, which, he states, began as a hard lump and gradually enlarged.

This lesion is painless, the size of a walnut, markedly infiltrated, papillomatous and reddened; a viscid discharge can be expressed from the center of the lesion. There are no palpable glands.

A roentgenogram of the lesion showed no abnormality. The Wassermann reaction was negative.

Granuloma Inguinale Involving the Buccal Cavity and the Inguinal Region. Presented by Dr. George Shropshear Jr. (by invitation).

M. A., a Negro aged 54, presents a raised linear granulomatous ulceration in the right inguinal region, about 1.5 cm. wide, extending downward to the femoroscrotal fold. The prepuce is edematous and phimotic, and its cutaneous surface is the site of an irregular ulcer. From both areas of ulceration a foul seropurulent discharge exudes. This process began in 1934, when it was more extensive than it is at present. The patient had adenitis of the right inguinal region in 1932; this subsided spontaneously.

Examination of the buccal cavity shows the teeth to be absent, while the gingivae, the palate, the buccal mucosa on the left side, the anterior pillars and the pharynx are the sites of soft, irregular, raised granulomatous involvement. There is no involvement of the tongue; the breath is fetid. This condition began in 1936, when difficulty in swallowing was experienced; ulceration of the palate followed. Later the teeth became loose and were extracted in May 1937.

The Kahn reaction was negative. The Frei test gave positive results. A smear of the discharge from the urethra showed gram-negative intracellular diplococci.

A histologic examination of both the inguinal region and the buccal cavity showed granulation tissue, while smears from the inguinal region and the palate, stained by Wright's method, showed Donovan bodies.

DISCUSSION

Dr. M. H. Ebert: This patient was at the Cook County Hospital for some time, and Donovan bodies were demonstrated in material from the inguinal lesion but not from the lesions in the mouth, although it was felt their origin was the same. Cases in which this disease affects the mouth have been reported. I presented a young girl some time ago because of granuloma inguinale in the popliteal folds. She had dermatitis in this area and the organisms probably were transferred by scratching.

Dr. H. Rattner: D. C. A Butts, in a series of cases of granuloma inguinale reported recently (*Am. J. Syph., Gonor. & Ven. Dis.* **21**:544, 1937), brought out the interesting point that practically all the patients had suffered from pediculosis pubis prior to the development of granuloma inguinale. The author suggested that this might be an important factor in the transmission of the disease—that an arthropod vector might be responsible for the spread of granuloma inguinale.

Addison's Disease in a Negro. Presented by Dr. E. A. Oliver and Dr. E. M. Smith Jr. (by invitation).

D. M., a Negro aged 35, was admitted to the St. Luke's Hospital on Oct. 7, 1937, with the following complaints: increasing weakness since 1927, which became progressively worse so that he had to stop work; increasing generalized pigmentation, which changed his color from brown to intense black; loss of 25 pounds (11 Kg.) during the past four years, and intolerance even to mild cold.

When he was first seen, in August 1934, his complaints included nausea, vomiting, weakness and marked hyperpigmentation. His blood pressure was 70 systolic and 50 diastolic, his temperature 94 F., and his pulse rate 76. Early in 1936 he had

been seen by Dr. Lawless, who gave him a total of 24 cc. of extract of adrenal cortex. This was followed by elevation of the blood pressure to 120 systolic and 90 diastolic.

In 1921 he had pleurisy in the left shoulder, which lasted for some time. He was admitted to the Cook County Hospital for diagnosis; from there he was sent to the City of Chicago Municipal Tuberculosis Sanitarium, where, he states, no evidence of pulmonary tuberculosis was found.

Examination showed extreme pigmentation of the skin, with areas on the buccal mucosa as well as on the hard palate and over the papillae of the tongue. The pigmentation did not resemble bronzing.

Examination of the blood showed 5,150,000 erythrocytes, 8,150 leukocytes and 80 per cent hemoglobin. The differential count showed 42 per cent polymorphonuclear neutrophils, 51 per cent lymphocytes, 2 per cent mononuclears and 4 per cent eosinophils. The Wassermann reaction was negative. The sedimentation rate was 23.5 mm. in one hour. The basal metabolic rate was —24.3 per cent. An electrocardiogram showed no abnormality. The urine was normal.

Intradermal injection of Stillians' solution (potassium ferricyanide and sodium thiosulfate) produced no change in color. Roentgenograms of the adrenal region showed two calcified areas which were interpreted to indicate calcification of the adrenal glands.

To estimate further the functional capacity of the patient, we placed him on a salt-free diet and gave him potassium by mouth, after which anorexia, vomiting and extreme weakness developed. This was overcome by the administration of salt, dextrose and extract of adrenal cortex.

The patient was placed on a diet and discharged from the hospital. He returned to the outpatient department markedly improved, with a blood pressure of 120 systolic and 80 diastolic, and was allowed to return to work. Some pain developed in his back, and he discontinued taking the salt. The symptoms returned. He is now taking salt again.

DISCUSSION

DR. S. W. BECKER: The pigmentation in Addison's disease is rather slowly progressive melanosis, which fits in well with the appearance of this patient. I think there is little doubt of the diagnosis of Addison's disease.

DR. PAUL A. O'LEARY, Rochester, Minn.: One point worthy of comment is that the type of involvement of the adrenal gland is not a factor in the degree of pigmentation. Some weeks ago my associates and I reported on a white patient in whom a completely generalized negroid pigmentation developed as a result of metastatic carcinomatous involvement of the adrenal glands. In the patient presented by Drs. Oliver and Smith the degree of increase in the pigmentation is similar to that in our case, but the pathologic process is probably tuberculous.

DR. THEODORE CORNBLEET: I noted that the concentration of cevitamic acid in the blood was 0.7 mg. per hundred cubic centimeters, which is definitely below the normal lower limit, of about 9.9 mg. The administration of vitamin C may cause absorption of the excess pigment in Addison's disease but without collateral measures will not change any other symptom or sign. I should like to suggest in addition to the high salt diet and the restriction of potassium, the administration of extract of adrenal cortex. Perhaps it would be too much to ask that a patient in the clinic be given this extract, because its high price is almost prohibitive. In cases in which the involvement is mild the high salt diet alone is sufficiently effective.

A Case for Diagnosis (Vesicular Pityriasis Rosea?). Presented by DR. M. H. EBERT and DR. THEODORE CORNBLEET.

E. F., a girl aged 16, has had a cutaneous eruption for twenty-seven days. The first lesion appeared on the right buttock four days prior to the other lesions. The lesions are fairly sharply defined crusted vesicular patches on the face, the trunk and the extremities. Many have their long axis in the direction of the

lines of cleavage. Others run in opposite directions, and some do not follow any particular direction. Many lesions, particularly on the forehead and the face, are infiltrated. The mouth is not involved. There was a lesion in the right palm, which at the present time is fading.

The lymp glands are not enlarged. The general physical examination showed no abnormality.

Examination of the blood showed 8,000 leukocytes. The differential count was essentially normal. The Wassermann test gave a negative result on two occasions. The urinalysis showed no abnormality.

DISCUSSION

DR. PAUL A. O'LEARY, Rochester, Minn.: I agree that many of the lesions are suggestive of pityriasis rosea but think that herpes gestationis should be borne in mind. I saw a woman through her first and part of her second pregnancy who during those periods presented a varied and bizarre picture of herpes gestationis, with lesions at times similar to the pityriasis rosea-like features present in the case under discussion. For therapy it might be well to give this patient intramuscularly some whole blood drawn from a woman during the menstrual period.

DR. OLIVER S. ORMSBY: This patient apparently has pityriasis rosea associated with vesicles. Such a condition is occasionally seen.

DR. DAVID LIEBERTHAL: The remarks of Dr. O'Leary are well taken. I am, however, inclined to consider this case one of toxic erythema which may have some connection with pregnancy.

DR. OTTO H. FOERSTER, Milwaukee: I agree with the diagnosis of a more or less vesicular type of pityriasis rosea, rather than that of impetigo herpetiformis, in which there is typical grouping of the lesions.

DR. M. H. EBERT: I feel that the picture is that of a rather unusual type of pityriasis rosea, especially in view of the fact that a patch developed over the buttock before the other patches appeared. However, it is questionable how much the condition can be considered to be modified by pregnancy. Some one stated he had seen a woman about four months pregnant with an almost identical eruption. I am going to follow Dr. O'Leary's suggestion of injecting whole blood from a menstruating woman and see if that treatment has any marked effect.

DR. OTTO H. FOERSTER, Milwaukee: According to the natural course of pityriasis rosea, the condition ought to clear up entirely in the next few weeks, and it would therefore be difficult to pass judgment on the effect of therapy.

Syphilis (Congenital), with Gumma of Face. Presented by DR. M. H. EBERT and DR. J. B. ROBBINS (by invitation).

S. A., a man aged 25, entered the Cook County Hospital on Sept. 21, 1937, with a destructive lesion involving the right cheek and both lips of eight weeks' duration.

The patient is congenitally syphilitic. At the age of 15 a gumma developed on the hard palate. During antisyphilitic therapy this cleared. Six years later another gumma developed in the nose. This healed during therapy, but the nose collapsed. In July 1937 he noticed a small nodule on the right cheek, which ulcerated and destroyed part of the right cheek and both lips. While the patient was in the hospital, ten injections of neoarsphenamine and five injections of bismuth subsalicylate in oil were administered. The gumma appeared to respond to therapy until about two weeks ago, when two small ulcerations appeared at the margin of the large defect.

The Wassermann reaction was 4 plus on Sept. 21, 1937. Urinalysis showed no abnormalities.

DISCUSSION

DR. OLIVER S. ORMSBY: Several times before I have mentioned a patient who had resistant syphilis that destroyed the nose, the upper lip and almost a third of

the face, in spite of constant treatment. After an injection of typhoid vaccine sufficient to produce a pronounced reaction, the condition responded favorably to injections of arsphenamine, which previously had not been effective.

DR. M. H. EBERT: I wish that Dr. Pusey were here, so that I could see if he would entertain the diagnosis of malignant syphilis in this case. The disease is rapidly spreading during the use of neoarsphenamine and of a bismuth preparation. The patient has had one injection of typhoid vaccine intravenously, but that was followed by no reaction.

DR. OLIVER S. ORMSBY: In the case I mentioned, in which what might be considered a shock injection of typhoid vaccine was administered, a severe reaction developed and there was marked elevation of temperature (to 106 F.), which immediately made the disease responsive to injections of arsphenamine. It appears necessary to induce considerable reaction before the reactivity of the affected tissues is changed.

DR. JAMES H. MITCHELL: I heard Dr. C. C. Dennie speak on the use of hot baths in such cases. He used a tub of hot water and raised the temperature to 104 F. He showed plates of a Charcot joint that had resisted all treatment and after a course of hot baths followed by arsenicals showed almost complete recovery.

DR. DAVID LIEBERTHAL: I remember a similar case of grave syphilis which Dr. Ormsby presented before this society at the occasion of a visit by Professor Dohi several years ago. In the present case I suggest a trial of compound decoction of sarsaparilla (Zittmann's decoction). It consists of two parts, a strong one and a mild one. They contain mostly numerous vegetable and some metallic ingredients. (MacGowan, G.: A Case of Malignant Syphilis Cured by Zittmann's Decoction, *J. Cutan. & Genito-Urin. Dis.* **19**:116, 1901. Keyes, E. L. Jr.: Syphilis, a Treatise for Practitioners, New York, D. Appleton & Co., 1908.)

NOTE: As the patient did not react to intravenous injections of typhoid vaccine, he was given gonococcus vaccine intravenously, followed by neoarsphenamine. This procedure produced good clinical results.

Hemangio-Endothelioma. Presented by DR. JOHN MILTON MCCUSKEY, Peoria, Ill.

I. M., a woman aged 49, stated that a pinhead-sized, slightly depressed lesion developed on the inner aspect of the left heel four years prior to her first visit, on Sept. 25, 1936. This lesion was covered with a crust, and occasionally there was a small amount of exudation. Seven months preceding the visit the lesion had increased to the size of a cherry, and two attempts were made to remove it, presumably by actual cautery. After the last treatment there was comparatively rapid growth, and the tumor bled occasionally.

At the age of 10 years the left heel had been punctured by a wire, but the wounds healed without visible scars. The patient is the mother of seven children. Menstruation stopped at the age of 47, and there has been no subsequent bleeding from the uterus. There was no history of jaundice. Her mother had epithelioma of the nose, and one grandfather was reported to have died from cancer.

Examination showed a well developed and well nourished woman. On the medial aspect of the left heel was a sharply defined tumor measuring 3.2 by 3.8 cm. It was elevated 1.5 cm. and was pedunculated, the diameter at the point of attachment being about one-half that of the tumor itself. The overhanging portion of the tumor rested on the underlying skin. It was moderately indurated and dull red and bled easily. The tumor was firmly attached to the underlying tissues. The draining lymph nodes were not palpable. The skin elsewhere was normal. Tissue of the tumor was obtained for microscopic examination, and a diagnosis of hemangio-endothelioma was made.

On September 7, eight radium implants, each containing 1.3 mg. of radium and having a well of platinum 0.5 mm. thick, were inserted into the tumor. These remained in place for ninety-six hours, for a total of 998.4 milligram hours of

irradiation. Within two months the tumor had almost entirely disappeared. However, the area then became infected, discharged purulent material and was painful. A roentgenogram of the heel and the foot revealed no pathologic changes of the bones. The ulcer had entirely healed by May 4, 1937. At the time of her next visit, three months later, the tissue at the site of the tumor appeared healthy, but her physical condition was entirely changed. She had lost about 30 pounds (13.6 Kg.), tired easily and complained of shortness of breath on exertion. There were several cherry-sized firm tumor masses in the region of the left femoral lymph nodes. A lemon-sized mass was palpable at the lower margin of the liver. Examination of the chest showed that most of the pulmonary tissue must be filled with metastatic lesions. No visible nodules were present in or beneath the skin. The patient died Sept. 30, 1937.

Autopsy showed a subcutaneous nodule on the right side of the forehead and one over the ninth rib. Each was about 6 mm. in diameter and firm. The gallbladder was large and tense and extended 5 cm. beyond the margin of the liver. The entire internal wall of the gallbladder presented soft masses projecting into the lumen in polypoid fashion. No tumor tissue was visible on the serous surface. A tumor was present in both the cystic and the hepatic duct, apparently causing complete obstruction of the cystic duct. The lungs were uniformly filled with hundreds of tumor nodules, varying from just visible ones to some 2 cm. in diameter. They were white, pale gray or hemorrhagic. Similar nodules were present in the pancreas and the left adrenal gland; a single nodule was found in the medulla of the right kidney. Some of the mesenteric and left femoral lymph nodes contained similar nodules. The uterus was slightly enlarged, but the external appearance was normal. The cavum was dilated and occupied by a lobulated tumor which originated in the endometrium of the fundus and projected downward into the cavum like a large, fleshy polyp. It measured 6 by 2 by 2 cm. and was gray with small hemorrhages.

Microscopic examination showed that all the tumor tissue, including the tumors of the heel, the gallbladder and the uterus and the nodules of the skin, the lungs, the pancreas, the kidney and the lymph nodes, had the same appearance. The tumor cells were spindle shaped; the nuclei were rather large and finely dotted with chromatin and usually contained a well demarcated nucleolus. Two characteristic arrangements of the cells were seen: 1. The more common of these consisted of whorls of cells. Usually in the center of the whorl there was a small capillary, and, while occasionally a flattened cell resembling an endothelial cell was seen, in most cases the tumor cells themselves made up the lining of the capillary. Large blood sinuses with concentric rings of tumor cells were present. These, too, were often lined by tumor cells themselves, although in some places separate endothelial cells were seen. 2. The other arrangement consisted of parallel sheafs of cells. Mitoses were present in moderate numbers.

The papillary masses in the gallbladder were made up of tumor cells which lay entirely between the muscularis and the widely separated covering epithelium. There was no apparent invasion of the muscularis or the serosa of the gallbladder. The tumor cells seemed to form smaller knots of cells than those seen elsewhere, and often the central blood vessel was absent. The covering epithelial cells of the gallbladder were normal. The polypoid masses in the uterus were made up of the same type of tumor tissue as that in the gallbladder and were confined to the endometrium, the myometrium being intact. The tumor nodules in the lungs and other organs were well demarcated and usually separated from the adjacent tissue by thin capsules. Multiple sections at the site of the tumor of the heel showed no tumor cells.

A histologic section of tumor tissue from various organs was presented for microscopic examination, as were photographs and photomicrographs.

Morphea with Pigmentation. Presented by Dr. S. J. Zakon (by invitation).

A Case for Diagnosis (Dermatitis Herpetiformis?). Presented by Dr. E. A. Oliver and Dr. W. W. Tobin (by invitation).

Book Reviews

Diseases of the Skin. A Manual for Students and Practitioners.—By the late Robert W. MacKenna, M.A., M.D., Ch.B. (Edinburgh, Scotland), sometime lecturer in dermatology at the University of Liverpool, England. Fourth edition, revised and enlarged by Robert M. B. MacKenna, M.A., M.D. (Cambridge), M.R.C.P. (London), Honorary Dermatologist, Royal Southern Hospital, Liverpool, England. Cloth, price, $7.50. Pp. 557, with 168 illustrations and 46 colored plates. Baltimore: William Wood & Company, 1937. Printed in England by William Clowes and Sons, of Beccles, England, for Bailliere, Tindall & Cox.

The most impressive features of this new book are the excellent clinical illustrations, the colored plates and the clear and concise presentation of the subject matter. The book is well assembled and contains an excellent index and an appendix. There are twenty-six chapters. The material is conveniently divided into three parts, concerning (1) diseases of known etiology; (2) those clinically similar, and (3) those affecting certain structures, for example, diseases of the hair.

The life history of Sarcoptes scabiei is new material and is accurately related. Many new diseases are not described. Even Kaposi's sarcoma is omitted. On the whole, the textbook is elementary and therefore suitable for medical students and general practitioners. For these two groups the author has taken pains to describe differential diagnosis fully. As a further aid to the student, excellent tables have been prepared, which enable the reader to separate one condition from another. The references are extremely scanty. The discussion of histopathologic material is brief. There are no photomicrographs of the common diseases, of Spirochaeta pallida or of basal or squamous cell epithelioma. The laboratory features of dermatology are not emphasized.

The chapter on erysipelas is well written, and the treatment described is modern. The same facts apply to the chapter on cutaneous tuberculosis. Gans' classification of tuberculosis of the skin is omitted. The chapter on syphilis is brief from the standpoint of clinical description. The portion of this chapter dealing with treatment could be fuller. No mention is made of the continuous and intermittent methods of treatment or of the method recommended by the League of Nations' committee. Tryparsamide is not mentioned.

On page 233 there is a formula for a preparation containing both mercury and sulfur. These two chemicals form a black sulfide of mercury and are not generally used in combination. On page 418 the use of solution of arsenic and mercuric iodides or of solution of potassium arsenite is recommended for the treatment of chronic psoriasis up to the point of causing albuminuria, gastrointestinal symptoms and puffiness of the eyelids. This is contrary to present day methods of treatment. The use of snake venom in the treatment of purpura is not described. The chapter on drug eruptions appears to be altogether too brief. Eruptions caused by such drugs as gold preparations, dinitrophenol, sulfanilamide and phenolphthalein are not discussed.

Physical medicine is an integral part of modern dermatology. Every effort should be made to evaluate properly the benefits of physical agents in the treatment of cutaneous diseases, especially when such agents are superior to all others. It is well that a modern dermatologic textbook expresses dosage of roentgen radiation in roentgens and not in pastilles. For the treatment of cavernous angioma, solid carbon dioxide is preferred to radium. Few if any dermatologists who are experts in the technic of electrolysis will agree with the author's opinion that the passage of an electric current through the skin stimulates lanugo hair

into activity. It must be remembered that electrolysis is the only method that will safely and permanently remove superfluous hair.

Dr. MacKenna's book cannot be considered a standard textbook.

The publishers are to be congratulated for their spendid choice of type and paper and for the excellence of reproduction of the illustrations and the colored plates.

Cutaneous Cancer and Precancer: A Practical Monograph. By George M. MacKee, M.D., and Anthony C. Cipollaro, M.D. Price, $3.75. Pp. 222, with 245 illustrations. New York: The American Journal of Cancer, 1937.

This monograph by Drs. MacKee and Cipollaro is invaluable. In chapter 1 the authors show that in approximately 6 per cent of deaths due to cancer the lesion originates in the skin or in the oral membranes. The remainder of the book shows how the mortality from this group of accessible cancers can be reduced.

In chapter 2 the authors have listed the precancerous dermatoses clearly and concisely. Every physician should be familiar with the chapter in which the authors describe lesions which in their clinical experience have proved to be potentially cancerous. The concise descriptions of the nineteen precancerous dermatoses are illustrated by clinical photographs of typical lesions, which should be useful to physicians in the early diagnosis of dangerous and often neglected diseases. The mortality from cancer would be greatly reduced if the danger signs were recognized early and proper treatment were instituted. It is this chapter that warrants distribution of this book to all physicians without regard to their specialty. The reduction in the mortality of accessible cancer is a grave responsibility for the medical profession, and the authors have given in this chapter much valuable assistance to physicians.

Chapter 3, on carcinoma and sarcoma, gives excellent descriptions and illustrations of malignant growths as they are seen clinically. There is nothing controversial in the classification or in the discussion of causes of malignant lesions. If, however, the reader is interested in pursuing any particular condition covered in this chapter or in chapter 2, he has only to turn to the bibliography, which contains references to 144 well chosen articles pertinent to chapter 2 and 162 references pertinent to chapter 3.

The recognized therapeutic methods are briefly reviewed in chapter 4. This discussion, with 29 references, should guide the experienced operator in the choice of a method for handling any condition described.

The monograph contains 212 pages, of which about half are taken up with selected photographs, clinical and microscopic. Too much praise cannot be given these well selected illustrations, and praise should be given to the Lancaster Press, Inc., for the excellent reproduction of the photographs, the type, the paper and the whole makeup of the book.

Theoretical Principles of Roentgen Therapy. Edited by E. A. Pohle. Price, $4.50. Pp. 271, with 132 illustrations. Philadelphia: Lea & Febiger, 1938.

This is a useful book for any one who uses roentgen rays as a therapeutic agent. The authors (Newell, Pohle, Stenstrom, Taylor and Wood) have surveyed the physical, technical, dosimetric, radiobiologic and radiopathologic branches and the matter of protection. Not only will the student and the beginner derive great advantage from this book, but the old-timer will be glad to have such a well arranged, intelligently written and exhaustive reference book. It can be recommended highly and the authors complimented.

The dermatologist will be especially interested in Dr. Wood's dermatologic studies, in which the rather complicated radiobiologic facts are skilfully condensed in a few pages.

There are two errors in printing which could be eliminated in the next edition: On page 40, the legend for figure 17 should read "6.4 mm. Al" instead of "3.2 mm. Al," and on page 42 the last line should read "1.38 AU."

Directory of Dermatologic Societies *

INTERNATIONAL

Tenth International Congress of Dermatology and Syphilology

Oliver S. Ormsby, President, 25 E. Washington St., Chicago.
Paul A. O'Leary, Secretary-General, 102–2nd Ave., S. W., Rochester, Minn.
Place: New York. Time: Summer 1940.

Pan American Medical Association, Section of Dermatology and Syphilology

Elmore B. Tauber, President, 19 W. 7th St., Cincinnati.
Austin W. Cheever, Secretary, 49 Bay State Rd., Boston.

FOREIGN

British Association of Dermatology and Syphilology (Canadian Branch)

J. J. McGovern, President, 4005 Dorchester St., Montreal.
F. L. Boulais, Secretary-Treasurer, 2061 St. Denis St., Montreal.

Royal Society of Medicine, Section of Dermatology

H. W. Barber, President, 7 Devonshire Pl., London, W. 1.
Louis Forman, Secretary, 7 Devonshire Pl., London, W. 1.

NATIONAL

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

Joseph V. Klauder, Chairman, 1934 Spruce St., Philadelphia.
J. Bedford Shelmire, Secretary, 1719 Pacific Ave., Dallas, Texas.
Place: San Francisco. Time: June 13-17, 1938.

American Academy of Dermatology and Syphilology

Howard Fox, President, 140 E. 54th St., New York.
Earl D. Osborne, Secretary, 471 Delaware Ave., Buffalo, N. Y.
Place: St. Louis. Time: November 1938.

American Board of Dermatology and Syphilology

Howard Fox, President, 140 E. 54th St., New York.
C. Guy Lane, Secretary, 416 Marlborough St., Boston.
Place: San Francisco. Time: June 1938.

American Dermatological Association

James Herbert Mitchell, President, 25 E. Washington St., Chicago.
Fred D. Weidman, Secretary, University of Pennsylvania, Philadelphia.
Place: Del Monte, Calif. Time: June 8-11, 1938.

Society for Investigative Dermatology

George M. MacKee, President, 200 W. 59th St., New York.
S. M. Becker, Secretary, University of Chicago, Department of Medicine, Chicago.

* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

SECTIONAL

Central States Dermatological Association

George H. Belote, President, University Hospital, Ann Arbor, Mich.
Thomas H. Miller, Secretary-Treasurer, 1305 David Whitney Bldg., Detroit.

Mississippi Valley Dermatological Society

A. H. Conrad, President, 3720 Washington Blvd., St. Louis.
Roy L. Kile, Secretary-Treasurer, 3720 Washington Blvd., St. Louis.

New England Dermatological Society

Fred S. Burns, President, 83 Marlborough St., Boston.
B. Appel, Secretary, 483 Beacon St., Boston.

Northern New Jersey Dermatological Society

Charles R. Mitchell, President, 311 Broadway, Paterson.
Louis J. B. LeBel, Secretary, 165 Grant Ave., Nutley.
Place: Academy of Medicine of Northern New Jersey, Newark. Time: Third Tuesday of March, April, October and December.

Southeastern Dermatological Association

J. L. Kirby-Smith, Chairman, 204 Laura St., Jacksonville, Fla.
Joseph A. Elliott, Secretary, Professional Bldg., Charlotte, N. C.

Southern Medical Association, Section on Dermatology and Syphilology

M. Toulmin Gaines, Chairman, 404 Merchants National Bank Bldg., Mobile, Ala.
Clinton W. Lane, Secretary, 508 N. Grand Ave., St. Louis, Mo.

STATE

California Medical Association, Scientific Assembly, Dermatology and Syphilology Section

Stanley O. Chambers, Chairman, 727 W. 7th St., Los Angeles.
Nelson Paul Anderson, Secretary, 2007 Wilshire Blvd., Los Angeles.
Place: Pasadena. Time: May 9-12, 1938.

Connecticut State Medical Society, Section on Dermatology

E. Myles Standish, Chairman, 179 Allyn St., Hartford.
Albert Levenson, Secretary, 881 Lafayette St., Bridgeport.
Place: New Haven. Time: May 19, 1938.

Florida Society of Dermatology and Syphilology

C. A. Andrews, Chairman, 706 Franklin St., Tampa.
Lauren Sompayrac, Secretary, 204 Laura St., Jacksonville.
Place: Jacksonville. Time: June 1938.

Louisiana Dermatological Society

M. T. Van Studdiford, President, 912 Pere Marquette Bldg., New Orleans.
R. A. Oriol, Secretary-Treasurer, 921 Canal St., New Orleans.

Massachusetts Medical Society, Section on Dermatology and Syphilology

George A. Dix, President, 6 Ashland St., Worcester.
J. Harper Blaisdell, Secretary, 45 Bay State Rd., Boston.

Medical Society of the State of New York, Section on Dermatology and Syphilology

Leo Spiegel, Chairman, 241 W. 100th St., New York.
Mark Heiman, Secretary, 600 Medical Arts Bldg., Syracuse.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA
SECTION ON DERMATOLOGY

L. G. Beinhauer, Chairman, 5026 Jenkins Arcade Bldg., Pittsburgh.
V. C. Garner, Secretary, Germantown Professional Bldg., Philadelphia.
Place: Scranton. Time: October 1938.

MICHIGAN STATE MEDICAL SOCIETY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

George Van Rhee, Chairman, 10 Peterboro St., Detroit.
Ruth Herrick, Secretary, 26 Sheldon Ave., S. E., Grand Rapids.

MINNESOTA DERMATOLOGICAL SOCIETY

L. A. Brunsting, President, 102–2d Ave., S. W., Rochester.
F. W. Lynch, Secretary-Treasurer, Lowry Medical Arts Bldg., St. Paul.
Time: First Friday in October, December, February and April.

OKLAHOMA STATE DERMATOLOGICAL SOCIETY

Harry Green, President, Medical Arts Bldg., Tulsa.
M. O. Nelson, Secretary, Medical Arts Bldg., Tulsa.

TEXAS DERMATOLOGICAL SOCIETY

Bedford Shelmire, President, 1719 Pacific Ave., Dallas.
Everett R. Seale, Secretary, 1215 Walker Ave., Houston.
Place: Galveston. Time: May 9-12, 1938.

LOCAL

BALTIMORE-WASHINGTON DERMATOLOGICAL SOCIETY

Herman E. Kittredge, President, 1835 I St., N. W., Washington, D. C.
I. Louis Sandler, Secretary, 1835 I St., N. W., Washington, D. C.
Place: Alternate cities. Time: Third Thursday of each month.

BRONX DERMATOLOGICAL SOCIETY

Theodore Rosenthal, President, 115 W. 86th St., New York.
Henry Silver, Secretary, 290 West End Ave., New York.
Time: June 1938.

BROOKLYN DERMATOLOGICAL SOCIETY

David L. Satenstein, President, 57 W. 57th St., New York.
M. Edward Goebel, Secretary, 842 Union St., Brooklyn.
Time: Third Monday of each month except June, July, August and September.

BUFFALO-ROCHESTER DERMATOLOGICAL SOCIETY

Clarence H. Peachey, President, 197 S. Goodman St., Rochester, N. Y.
Richard L. Saunders, Secretary, 333 Linwood Ave., Buffalo.

CENTRAL NEW YORK DERMATOLOGICAL SOCIETY

Rudolph Ruedemann Jr., President, 256 State St., Albany.
Harry D. Parkhurst, Secretary-Treasurer, 264 Genesee St., Utica, N. Y.

CHICAGO DERMATOLOGICAL SOCIETY

Hamilton Montgomery, President, Mayo Clinic, Rochester, Minn.
Herbert Rattner, Secretary, 25 E. Washington St., Chicago.
Place: Chicago. Time: Third Wednesday in January 1938.

CINCINNATI DERMATOLOGICAL SOCIETY

Leon Goldman, President, Doctors Bldg., Cincinnati.
George E. Clarke, Secretary-Treasurer, 19 W. 7th St., Cincinnati.
Place: Cincinnati. Time: First Wednesday of each month, except June, July, August and September.

Cleveland Dermatological Society

Claude B. Norris, President, 244 Lincoln Ave., Youngstown, Ohio.
Clyde L. Cummer, Secretary, 1010 Hanna Bldg., Cleveland.
Place: Cleveland. Time: May 26, 1938.

Detroit Dermatological Society

George H. Belote, President, University Hospital, Ann Arbor, Mich.
Thomas H. Miller, Secretary-Treasurer, 1305 David Whitney Bldg., Detroit.
Place: Detroit. Time: May 1938.

Los Angeles Dermatological Society

Thomas W. Nisbet, President, 65 N. Madison Ave., Pasadena, Calif.
C. R. Caskey, Secretary, 1930 Wilshire Blvd., Los Angeles.
Time: Second Tuesday of each month, October to May, inclusive.

Manhattan Dermatologic Society

Andrew J. Gilmour, Chairman, 121 E. 60th St., New York.
Anthony C. Cipollaro, Secretary, 40 E. 61st St., New York.
Place: New York. Time: May 1938.

Montreal Dermatological Society

B. Usher, President, 1538 Sherbrooke St., W., Montreal, Canada.
Paul Poirier, Secretary, 450 Sherbrooke St., E., Montreal, Canada.

New York Academy of Medicine, Section of Dermatology and Syphilis

Louis Chargin, Chairman, 1 W. 85th St., New York.
Harry C. Saunders, Secretary, 159 W. 87th St., New York.

New York Dermatological Society

Eugene F. Traub, President, 140 E. 54th St., New York.
Frank C. Combes, Secretary, 80 W. 40th St., New York.

Omaha Dermatological Society

Donald J. Wilson, President, 1113 Medical Arts Bldg., Omaha.
Leonard J. Owen, Secretary-Treasurer, 954 Stuart Bldg., Lincoln.

Philadelphia Dermatological Society

Frank C. Knowles, Chairman, 2035 Spruce St., Philadelphia.
Thomas Butterworth, Secretary, 411 Walnut St., Reading, Pa.
Time: Third Friday of each month from September to May, inclusive.

Pittsburgh Dermatological Society

A. Fisher, President, 530½–5th Ave., McKeesport, Pa.
Francis P. Kenney, Secretary, Westinghouse Bldg., Pittsburgh.

St. Louis Dermatological Society

A. H. Conrad, President, 3720 Washington Blvd., St. Louis.
Roy L. Kile, Secretary-Treasurer, 3720 Washington Blvd., St. Louis.
Place: Barnard Free Skin and Cancer Hospital. Time: 2 p. m., second Wednesday of each month.

San Francisco Dermatological Society

Norman Epstein, President, 450 Sutter St., San Francisco.
H. V. Allington, Secretary, 3115 Webster St., Oakland.
Place: San Francisco. Time: Third Friday of November 1937.